

=> E NOMURA MASAHIRO/AU 25
E1 5 NOMURA MASAHIDE/AU
E2 77 NOMURA MASAHIKO/AU
E3 138 --> NOMURA MASAHIRO/AU
E4 1 NOMURA MASAHIRO S/AU
E5 4 NOMURA MASAHISA/AU
E6 1 NOMURA MASAHORI/AU
E7 1 NOMURA MASAICHIRO/AU
E8 1 NOMURA MASAITI/AU
E9 20 NOMURA MASAJI/AU
E10 2 NOMURA MASAKASTU/AU
E11 344 NOMURA MASAKATSU/AU
E12 38 NOMURA MASAKAZU/AU
E13 40 NOMURA MASAKI/AU
E14 7 NOMURA MASAKO/AU
E15 11 NOMURA MASAMI/AU
E16 2 NOMURA MASAMICHI/AU
E17 6 NOMURA MASANAO/AU
E18 1 NOMURA MASANARI/AU
E19 1 NOMURA MASANIRO/AU
E20 2 NOMURA MASANO/AU
E21 4 NOMURA MASANOBU/AU
E22 12 NOMURA MASANORI/AU
E23 143 NOMURA MASAO/AU
E24 2 NOMURA MASAOMI/AU
E25 1 NOMURA MASARO/AU

=> S (E2 OR E3 OR E4) AND (BENZYLTHIA?)

77 "NOMURA MASAHIKO"/AU
138 "NOMURA MASAHIRO"/AU
1 "NOMURA MASAHIRO S"/AU
227 BENZYLTHIA?

L7 3 ("NOMURA MASAHIKO"/AU OR "NOMURA MASAHIRO"/AU OR "NOMURA MASAHIRO S"/AU) AND (BENZYLTHIA?)

=> S (E2 OR E3 OR E4) AND (LIPID?)

77 "NOMURA MASAHIKO"/AU
138 "NOMURA MASAHIRO"/AU
1 "NOMURA MASAHIRO S"/AU
277666 LIPID?

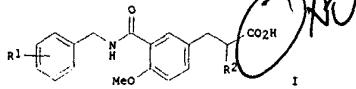
L8 11 ("NOMURA MASAHIKO"/AU OR "NOMURA MASAHIRO"/AU OR "NOMURA MASAHIRO S"/AU) AND (LIPID?)

=> DIS L8 1 IBIB ABS

THE ESTIMATED COST FOR THIS REQUEST IS 2.29 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L8 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2002428859 CAPLUS
 DOCUMENT NUMBER: 137:5998
 TITLE: Preparation of (phenylmethyl)alkanoic acid derivatives
 as PPAR_{alpha} agonists for treatment of arteriosclerosis, obesity, diabetes, etc.
 INVENTOR(S): Miyachi, Hiroyuki; Nomura, Masahiro; Takahashi, Yukie; Tanase, Takahiro; Murakami, Kouji
 PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 52 pp.
 CODEN: PIXKD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002044130	A1	20020606	WO 2001-JP10353	20011128
W: AE, AG, AL, AM, AT, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, GE, GH, LK, LR, OM, PH, TZ, UA, TJ, TM	CO, CR, CU, CY, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, RW: GH, GM, KE, LS, MN, MZ, SD, SL, SZ, T2, UG, ZM, ZW, AT, BE, CH, SE, TR, TD, TG	DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, BF, BJ, CF, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, JR 2000-363677 A 20001129		
PRIORITY APPN. INFO.: MARPAT 137:5998	GI			
OTHER SOURCE(S):				



AB The title compds. I [R1 represents hydrogen, halogeno, hydroxy, 2-phenylethyl, 2-phenoxyethoxy, hydroxyphenoxy or benzyloxyphenoxy; and R2 represents lower (C1-4) alkyl] are prep'd. I are lipid-lowering

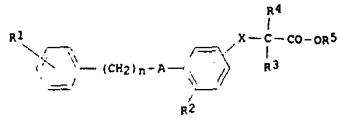
L8 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2002 ACS (Continued)
 drugs (particularly in the liver), drugs preventing the progress of arteriosclerosis, anti-obesity drugs and remedies for diabetes.
 For example, 2-[3-(N-[(4-chlorophenyl)methyl]carbamoyl)-4-methoxyphenyl]methylbutyric acid (II) was prep'd. The PPAR_{alpha} agonist activity of II was demonstrated.
 REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2002:428856 CAPLUS
 DOCUMENT NUMBER: 137:20225
 TITLE: Preparation of phenylmethylalkanoic acid
 derivatives
 treatment of hyperlipidemia, arteriosclerosis, diabetes, and
 obesity
 INVENTOR(S): Miyachi, Hiroyuki; Nomura, Masahiro;
 Murakami, Kouji
 PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 67 pp.
 CODEN: PIKKD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

b. b. 02

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002044127	A1	20020606	WO 2001-JP10355	20011128
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:	JP 2000-363679	A 20001129		
OTHER SOURCE(S):	MARPAT 137:20225			
GI				

L8 ANSWER 2 OF 11 CAPLUS COPYRIGHT 2002 ACS (Continued)
 phenoxy, etc.; R2 represents hydrogen or lower alkoxy; R3, R4 and
 R5 represent each hydrogen or lower alkyl; A represents NHCO or CONH;
 X is located at the para-position relative to A and represents oxygen or
 sulfur, or X is located at the para-position relative to R2 and
 represents oxygen or sulfur; and n is an integer of from 0 to 2], useful as
 PPAR.alpha. agonists (no data) for the treatment of hyperlipidemia,
 arteriosclerosis, diabetes, and obesity, are prepd. For example,
 2-[(4-N-[(4-(trifluoromethyl)phenyl)methyl]carbamoyl)-3-
 methoxyphenyl]methyl]butyric acid was prepd.
 REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT



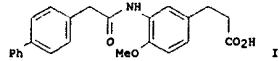
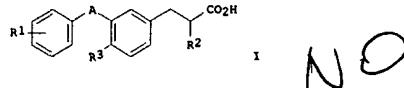
AB The title compds. I [R1 represents trifluoromethyl, optionally substituted]

NO

L8 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001886030 CAPLUS
 DOCUMENT NUMBER: 136:19941
 TITLE: Preparation of phenylpropionic acid
 derivatives as
 PPAR.alpha. activators effective as
 antiarteriosclerotics
 INVENTOR(S): Miyachi, Hiroyuki; Nomura, Masahiro;
 Takahashi, Yukie; Tanase, Takahiro; Murakami,
 Kouji;
 Suzuki, Masahiro
 PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 115 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001092201	A1	20011206	WO 2001-JP4385	20010525
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			JP 2000-158424	A 20000529
OTHER SOURCE(S):	MARPAT 136:19941			
GI				

L8 ANSWER 3 OF 11 CAPLUS COPYRIGHT 2002 ACS (Continued)



AB Title compds. [I: R1 = alkyl, alkoxy, trifluoromethyl, trifluoromethoxy, Ph, phenoxy, benzyloxy; R2 = H, alkyl, alkoxy; R3 = alkoxy; A = CH₂CONH, NHCOCH₂, CH₂CH₂CO, CH₂CH₂CH₂, CH₂CH₂O, CONHCH₂, CH₂NHCH₂, COCH₂O, OCH₂CO, COCH₂NH, NHCH₂CO], stereoisomers, and pharmaceutically acceptable salts, which bind to human peroxisome proliferator activated receptor .alpha. (PPAR.alpha.) as ligand to activate the receptor and thereby exhibit a potent lipid-decreasing effect, are prep'd. as antiarteriosclerotics. Thus, the title compd. II was prep'd. and biol. tested for transcription activation effect with EC₅₀(μmol/L) = 0.05. REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

No

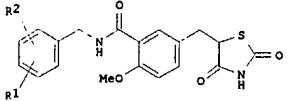
L8 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:51907 CAPLUS
DOCUMENT NUMBER: 136:256870
TITLE: Effects of idoxifene and estradiol on
NF-.kappa.B activation in cultured rat hepatocytes
undergoing oxidative stress
AUTHOR(S): Omoya, Toshihiro; Shimizu, Ichiro; Zhou, Yajun;
Okamura, Yoshihito; Inoue, Hiroshi; Lu,
Guangming;
COPARTNERS: Itonaga, Mine; Honda, Norimura,
Masahiro; Ito, Susumu
CORPORATE SOURCE: Second Department of Internal Medicine,
Tokushima
University School of Medicine, Tokushima,
770-8503,
Japan
SOURCE: Liver (Copenhagen, Denmark) (2001), 21(3),
183-191
PUBLISHER: Munksgaard International Publishers Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Background/Aims: Idoxifene is a tissue-specific selective estrogen receptor modulator. Estradiol is a potent endogenous antioxidant, and nuclear factor .kappa.B (NF-.kappa.B) is a key transcription factor that induces multiple genes in response to inflammation or oxidative stress. The aim of this study was to explore the inhibitory effects of idoxifene and estradiol on NF-.kappa.B activation in hepatocytes in a state of oxidative stress. Methods: Lipid peroxidn. was induced in cultured rat hepatocytes by incubation with ferric nitrilotriacetate soln. NF-.kappa.B activity was evaluated by electrophoretic mobility shift assay. Results: The oxidative stress-induced activation of NF-.kappa.B and degrdn. of I.kappa.B-.alpha. were maximal at 3-5 h, with an increase in lactate dehydrogenase (LDH) and malondialdehyde (MDA) secretion into the culture medium. Treatment with idoxifene and estradiol inhibited I.kappa.B-.alpha. degrdn. and NF-.kappa.B activation through the attenuation of hepatocyte oxidative bursts and decreased extracellular levels of LDH and MDA. In addn., idoxifene and estradiol inhibited lipid peroxidn. in rat liver mitochondria. A potent NF-.kappa.B inhibitor, pyrrolidine dithiocarbamate, prevented NF-.kappa.B activation by inhibition of I.kappa.B-.alpha. degrdn. and decreased LDH and MDA

L8 ANSWER 4 OF 11 CAPLUS COPYRIGHT 2002 ACS (Continued)
levels, suggesting that NF-.kappa.B might be a regulator in a genetic response to increase oxidative stress-induced hepatic injury. Conclusions: These findings suggest that idoxifene and estradiol function as antioxidants and protect hepatocytes from inflammatory cell injury.
REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

NO

L8 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:152661 CAPLUS
 DOCUMENT NUMBER: 134:193428
 TITLE: Preparation of substituted
 benzylthiazolidine-2,4-
 dione derivatives as agonists of human
 peroxisome
 proliferator-activated receptor
 INVENTOR(S): Nomura, Masahiro; Murakami, Koji; Tsunoda,
 Masaki; Takahashi, Yukie
 PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 19 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014352	A1	20010301	WO 2000-JP5522	20000818
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, ME, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG EP 1207158		EP 2000-953478	20000818	
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL		JP 1999-235530	A 19990823	
PRIORITY APPLN. INFO.:		WO 2000-JP5522	W 20000818	
OTHER SOURCE(S): MARPAT 134:193428 GI				



L8 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2002 ACS (Continued)
 AB The title compds. (I), pharmaceutically acceptable salts thereof
 and hydrates of the same (wherein R1 represents chloro, bromo, nitro,
 trifluoromethoxy, ethoxy, propoxy or isopropoxy; and R2 represents
 hydrogen or chloro) are prep'd. These compds. are capable of, as a
 ligand
 of human peroxisome proliferator-activated receptor (PPAR),
 enhancing the transcriptional activity of the receptor and showing effects of
 lowering
 blood sugar level and lowering lipid level; and a process for
 producing the same. Thus, 5-[(2,4-dioxothiazolidin-5-yl)methyl]-2-
 methoxybenzoic acid, Et3N, and CH2Cl2 were mixed, treated with Et
 chlorocarbonate and stirred under ice-cooling for 10 min, treated
 with 4-nitrobenzylamine, and then stirred at room temp. for 2 h to give
 75t
 N-[(4-nitrophenyl)methyl]-5-[(2,4-dioxothiazolidin-5-yl)methyl]-2-
 methoxybenzamide (II). II and I (R1 = 4-n-Pro, R2 = H) enhanced
 the transcriptional activity of human PPAR. α . in CHO cells with
 EC50 of
 0.53 and 0.11 .mu.M, resp.
 REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE
 FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L8 ANSWER 6 OF 11 CAPIUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001152660 CAPIUS

DOCUMENT NUMBER: 134:193427

TITLE: Preparation of substituted

benzylthiazolidine-2,4-dione derivatives as agonists of human

peroxisome

proliferator-activated receptor

INVENTOR(S): Miyachi, Hiroyuki; Nomura, Masahiro; Tanase, Takahiro; Murakami, Koji; Tsunoda, Masaki

PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 20 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

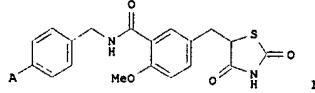
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014351	A1	20010301	WO 2000-JP5521	20000818
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, ID, IL, LV, MD, SI, SK, AZ, BY,	CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, IN, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, MG, MK, MN, MW, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, BF, BJ,	CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG EP 1207157	A1 EP 2000-953477	20000818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL	JP 1999-235529 A 19990823 JP 2000-242707 A 20000810 WO 2000-JP5521 W 20000818			

OTHER SOURCE(S): MARPAT 134:193427

GI

L8 ANSWER 6 OF 11 CAPIUS COPYRIGHT 2002 ACS (Continued)
AB The title compds. represented by general formula (I); wherein A
represents
optionally substituted Ph, optionally substituted phenoxy or
optionally substituted benzoyloxy), pharmaceutically acceptable salts thereof
and
hydrates of the same are prep'd. These compds. are capable of, as
a ligand
of human peroxisome proliferator-activated receptor (PPAR),
enhancing the
transcriptional activity of the receptor and showing effects of
lowering
blood sugar level and lowering lipid level. Thus,
5-[(2,4-dioxothiazolidin-5-yl)methyl]-2-methoxybenzoic acid, Et3N,
and
CH2Cl2 were mixed, treated with Et chlorocarbonate under
ice-cooling, and
stirred for 10 min under ice-cooling, followed by adding a soln. of
4-benzoyloxybenzylamine in CH2Cl2, and the resulting mixt. was
stirred at
room temp. for 2 h to give 77%
N-[(4-benzoyloxyphenyl)methyl]-5-[(2,4-
dioxothiazolidin-5-yl)methyl]-2-methoxybenzamide (II). II and I
(A = PhO)
enhanced the transcriptional activity of human PPAR. α . in CHO
cells
with EC50 of 0.44 and 0.24 .mu.M, resp.
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE
FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT



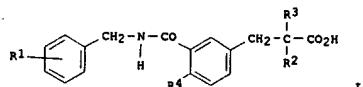
L8 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:881114 CAPLUS
 DOCUMENT NUMBER: 134:29211
 TITLE: Preparation of
 phenylmethylcarbamoylphenylpropionic
 acid derivatives as human peroxisome
 proliferator-activated receptor- α .
 (PPAR- α .)
 INVENTOR(S): agonists
 Nomura, Masahiro; Takahashi, Yukie; Tanase,
 Takahiro; Miyachi, Hiroyuki; Tsunoda, Masaki;
 Ide,
 PATENT ASSIGNEE(S): Tomohiro; Murakami, Koji
 Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 90 pp.
 CODEN: PIKXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000075103	A1	20001214	WO 2000-JP3707	20000608
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG JP 2001055367 A2 20010227 JP 2000-157600 20000529 BR 2000011734 A 20020305 BR 2000-11734 20000608 EP 1184366 A1 20020306 EP 2000-935582 20000608 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO NO 200106001 A 20020211 NO 2001-6001 20011207 PRIORITY APPLN. INFO.: JP 1999-162235 A 19990609 BR 2000-157600 A 20000529 WO 2000-JP3707 W 20000608				

OTHER SOURCE(S): MARPAT 134:29211

GI

L8 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2002 ACS (Continued)



AB The title compds. I [R1 = alkyl, etc.; R2 = alkyl, alkoxy, etc.; when R2 is alkyl, 2,2,2-trifluoroethyl, R3 is H, alkyl; when R2 is alkoxy, phenoxy, etc., R3 is H; R4 = alkoxy] are prepd. I activate the PPAR- α receptors and lower blood lipid (cholesterol and neutral lipid) levels. 2-Ethyl-3-[4-methoxy-3-[N-[(4-(trifluoromethyl)phenyl)methyl]carbamoyl]phenyl]propionic acid at 30 mg/kg gave 55% decrease in total cholesterol in rats.
 REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 1997:116453 CAPLUS

DOCUMENT NUMBER: 126:157499

TITLE: Preparation of N-substituted

dioxothiazolidylbenzamide

INVENTOR(S): derivatives as blood sugar lowering agents
Maeda, Toshio; Nomura, Masahiro; Awano,
Katsuwa; Kinoshita, Susumu; Sato, Hiroya;

Murakami,

PATENT ASSIGNEE(S): Koji; Tsunoda, Masaki
Kyorin Seiyaku KK, Japan.
Jpn. Kokai Tokkyo Koho, 11 pp.

SOURCE: CCON: JXXXAF

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

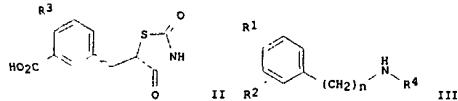
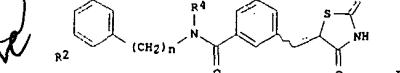
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PARENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 08333355	A2	19961217	JP 1995-159782	19950602

OTHER SOURCE(S): MARPAT 126:157499

GI



AB The title compds. (I; R1, R2 = H, Cl-4 alkyl, Cl-3 alkoxy, haloalkoxy, or haloalkyl, halo, OH, NO₂, etc.; R3 = H, Cl-3 alkoxy, halo, OH; R4 = H, Cl-4 alkyl; dotted line = single or double bond; n = 0-2) are prep'd. by reacting benzoic acid derivs. (II; R3, dotted line = same as above) with amines (III; R1, R2, R4, n = same as above). I, possessing blood sugar and lipid lowering activities, are useful for diabetes mellitus and hyperlipemia. Thus, 5-(2,4-dioxothiazolidyl-5-ylidene)methyl-2-

methoxybenzoic acid was reacted with 4-tert-butylaniline in the presence

of Et₃N and NCP(O)(OEt)₂ to give 99% I (R1 = 4-tert-BuC₆H₄, R3 =2-MeO, R2 = R4 = H, dotted line = double bond, n = 0). I (R1 = R2 = 4-CP₃,

R3 = 6-MeO, R4 = Et, dotted line = single bond, n = 1) at 10 mg/kg

showed 31% blood sugar lowering activity when tested on mouses p.o. in vivo.

showed 31%

blood sugar lowering activity when tested on mouses p.o. in vivo.

same assignee

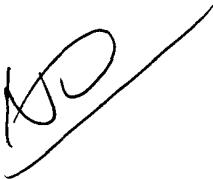
103?

balance on lipid compositions and learning ability of rats. II. Discrimination process, extinction process, and glycolipid compositions Yamamoto, Nobuhiro; Hashimoto, Atsushi; Takemoto, Yasuhiko; Okuyama, Harumi; Nomura, Masahiko; Kitajima, Rie; Togashi, Takako; Tamai, Yoichi; Fac. Pharm. Sci., Nagoya City Univ., Nagoya, 467, Japan
 SOURCE: J. Lipid Res. (1988), 29(8), 1013-21
 CODEN: JLIPRAW; ISSN: 0022-2275
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Donryu strain rats through 2 generations were fed semi-purified diets supplemented with safflower seed oil (rich in linoleic acid) or perilla seed oil (rich in .alpha.-linolenic acid) or fed a conventional lab. chow (normal control diet). The brightness-discrimination learning ability was highest in the perilla oil-fed group, followed by the normal group, and then by the safflower group, extending the earlier observation in a different strain of rat that .alpha.-linolenic acid is a factor in maintaining high learning ability (Yamamoto, N. et al., 1987). After the brightness-discrimination learning test was administered, extinction of learning was measured. The time required for extinction was significantly longer in the safflower group than in either the perilla group or the normal diet group. Thus, the dietary .alpha.-linolenate/linoleate balance affected both learning and the extinction of learning. The glycolipids of the cerebrum, cerebellum, and olfactory lobe were analyzed. Although the fatty acid compns. of the sulfatide and gangliosides were significantly different in the 3 parts of the brain, relatively little difference was obse. in the fatty acids of glycolipids between the safflower group and the perilla group, suggesting that gross changes in brain glycolipids are not responsible for the differences in learning abilities between these dietary groups.

L8 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1987:195209 CAPLUS
DOCUMENT NUMBER: 106:195209
TITLE: Effect of dietary .alpha.-linolenate/linoleate balance
on brain lipid compositions and learning ability of rats
AUTHOR(S): Yamamoto, Nobuhiro; Saito, Masaki; Moriuchi, Atsuko
CORPORATE SOURCE: Nomura, Masahiko; Okuyama, Harumi
467, Fac. Pharm. Sci., Nagoya City Univ., Nagoya,
SOURCE: Japan
J. Lipid Res. (1987), 28(2), 144-51
DOCUMENT TYPE: CODEN: JLPRAW ISSN: 0022-2275
LANGUAGE: English
AB Spontaneously hypertensive rats (SHR) and normotensive control, Wistar/Kyoto (WKY) rats through two generations were fed a semipurified diet supplemented either with safflower oil (rich in linoleate [n-6-33-3]) or with perilla oil (rich in .alpha.-linolenate [463-40-1]). The cerebral lipid contents and phospholipid compns. did not differ between the two dietary groups of SHR rats. There were also no differences in the unsatd./satd. ratios of individual phospholipids or the proportions of plasmalogens. However, the proportions of n-3 and n-6 fatty acids were significantly different. Decreases in the proportions of docosahexaenoate [22:6 (n-3)] [6217-54-5] in phosphatidylethanolamine and phosphatidylserine in the safflower oil group were compensated for with increases in the proportions of docosatetraenoic acid [22:4 (n-6)] [28874-58-0] and docosapentaenoic acid [22:5 (n-6)] [25182-74-5] as compared with the perilla oil group. These differences in phospholipidacyl chains were much smaller than the difference in the proportions of linoleate and .alpha.-linoleate of the diets. In a brightness-discrimination learning test, the total no. of responses to the pos. and neg. stimuli were less in the groups fed perilla oil. However, the .alpha.-linolenate-deficient group took longer to decrease the frequency of R- responses and therefore longer to learn the discrimination. Consequently, the correct response ratios were higher in the perilla oil groups than in the safflower oil groups. Thus, the dietary .alpha.-linolenate/linoleate balance influenced the (n-3)/(n-6) balance of polyenoic fatty acids differently among brain phospholipids. These changes in fatty acid compn. were accompanied by changes in the

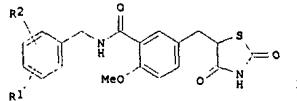
L8 ANSWER 10 OF 11 CAPLUS COPYRIGHT 2002 ACS (Continued)
brightnes-discrimination learning ability in SHR and WKY rats, with rats fed a diet enriched in .alpha.-linolenate being superior in the correct response ratio.

L8 ANSWER 11 OF 11 CAPIUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1986:51A062 CAPIUS
DOCUMENT NUMBER: 105:114062
TITLE: Effects of dl-.alpha.-tocopherol on lipid
peroxide
AUTHOR(S): Ebisu, Hiroshi; Koide, Tadashi; Nomura,
Masahiko; Nagata, Yutaka
CORPORATE SOURCE: Res. Off., Fukuyukai Hosp., Aichi, Japan
SOURCE: Igeku to Seibutsugaku (1985), 111(6), 343-6
CODEN: IGSBAL; ISSN: 0019-1604
DOCUMENT TYPE: Journal
LANGUAGE: Japanese
AB In mice fed with a high-lipid diet, the concns. of lipid
peroxides in the heart of animals injected with
dl-.alpha.-tocopherol
[2074-53-5] (15.0 mg/100 g) were lower than those in mice without
dl-.alpha.-tocopherol.

A handwritten signature consisting of stylized, cursive letters, likely reading "H. Ebisu". It is positioned above a diagonal line.

L12 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:152661 CAPLUS
 DOCUMENT NUMBER: 134:193428
 TITLE: Preparation of substituted benzylthiazolidine
 -2,4-dione derivatives as agonists of human
 peroxisome
 proliferator-activated receptor
 INVENTOR(S): Nomura, Masahiro; Murakami, Koji; Tsunoda,
 Masaki; Takahashi, Yukie
 PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 19 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014352	A1	20010301	WO 2000-JP5522	20000818
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CR, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG EP 1207158		A1	20020522	EP 2000-953478 20000818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
PRIORITY APPLN. INFO.: JP 1999-235530 A 19990823				
OTHER SOURCE(S): MARPAT 134:193428			WO 2000-JP5522	W 20000818
GI				



AB The title compds. (I), pharmaceutically acceptable salts thereof and

L12 ANSWER 1 OF 4 CAPLUS COPYRIGHT 2002 ACS (Continued)
 hydrates of the same (wherein R1 represents chloro, bromo, nitro, trifluoromethoxy, ethoxy, propoxy or isopropoxy; and R2 represents hydrogen or chloro) are prep'd. These compds. are capable of, as a ligand
 of human peroxisome proliferator-activated receptor (PPAR),
 enhancing the
 transcriptional activity of the receptor and showing effects of
 lowering
 blood sugar level and lowering lipid level; and a process for
 producing
 the same. Thus,
 5-[(2,4-dioxothiazolidin-5-yl)methyl]-2-methoxybenzoic
 acid, Et3N, and CH2Cl2 were mixed, treated with Et chlorocarbonate
 and
 stirred under ice-cooling for 10 min, treated with
 4-nitrobenzylamine, and
 then stirred at room temp. for 2 h to give 75%
 N-[(4-nitrophenyl)methyl]-5-
 [(2,4-dioxothiazolidin-5-yl)methyl]-2-methoxybenzamide (II). II
 and I (RI
 = 4-n-Pro, R2 = H) enhanced the transcriptional activity of human
 PPAR.alpha. in CHO cells with EC50 of 0.53 and 0.11 .mu.M, resp.
 REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE
 FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

371/6
 PCT

L12 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001152660 CAPLUS

DOCUMENT NUMBER: 134:193427

TITLE: Preparation of substituted benzylthiazolidine
-2,4-dione derivatives as agonists of human

peroxisome

INVENTOR(S): Miyachi, Hiroyuki; Nomura, Masahiro; Tanase,

Takahiro;

PATENT ASSIGNEE(S): Murakami, Koji; Tsunoda, Masaki

Kyorin Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 20 pp.

CODEN: PIKXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

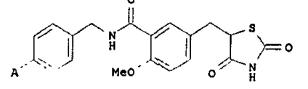
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014351	A1	20010301	WO 2000-JP5521	20000818
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, ID, IL, LV, MD, SI, SK, AZ, BY, CH, CY, BF, BJ,	C2, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1207157	A1	20020522	EP 2000-953477	20000818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			JP 1999-235529 A 19990823	
PRIORITY APPLN. INFO.:			JP 2000-242707 A 20000810	
			WO 2000-JP5521 W 20000818	

OTHER SOURCE(S): MARPAT 134:193427

GI



NO

L12 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2002 ACS (Continued)

AB The title compds. represented by general formula (I); wherein A represents
optionally substituted Ph, optionally substituted phenoxy or
optionally substituted benzyloxy), pharmaceutically acceptable salts thereof
and
hydrates of the same are prepd. These compds. are capable of, as
a ligand
enhancing the
transcriptional activity of the receptor and showing effects of
lowering
blood sugar level and lowering lipid level. Thus, 5-[(2,4-
dioxothiazolidin-5-yl)methyl]-2-methoxybenzoic acid, Et3N, and
CH2Cl2 were
mixed, treated with Et chlorocarbonate under ice-cooling, and
stirred for
10 min under ice-cooling, followed by adding a soln. of
4-benzyloxybenzylamine in CH2Cl2, and the resulting mixt. was
stirred at
room temp. for 2 h to give 77%
N-[(4-benzyloxyphenyl)methyl]-5-[(2,4-
dioxothiazolidin-5-yl)methyl]-2-methoxybenzamide (II). II and I
(A = PhO)
enhanced the transcriptional activity of human PPAR. α . in CHO
cells
with EC50 of 0.44 and 0.24 μ M, resp.

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE

FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

NO

NO

L12 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:152659 CAPLUS
 DOCUMENT NUMBER: 134:178551
 TITLE: Preparation of substituted benzylthiazolidine
 -2,4-dione derivatives as ligands of human
 peroxisome
 INVENTOR(S): Fujimori, Shizuyoshi; Murakami, Koji;
 Tsunoda, Masaki
 PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 18 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014350	A1	20010301	WO 2000-JP5520	20000818
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CR, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG EP 1207156		A1 20020522	EP 2000-953476	20000818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL		JP 1999-235528	A 19990823	
PRIORITY APPN. INFO.: WO 2000-JP5520		W 20000818		

GI



AB The title compds. (I; wherein A represents pyridyl or cyclohexyl), pharmaceutically acceptable salts thereof and hydrates of the same are

L12 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2002 ACS (Continued)
 prep'd. These compds. are capable of, as a ligand of human
 peroxisome
 proliferator-activated receptor (PPAR), enhancing the
 transcriptional
 activity of the receptor and showing effects of lowering blood
 sugar level
 and lowering lipid level. Thus,
 5-((2,4-dioxothiazolidin-5-yl)methyl)-2-
 methoxybenzoic acid, 2-picolyamine, 1-ethyl-3-(3-
 dimethylaminopropyl)carbodiimide hydrochloride, and DMF were
 stirred at
 room temp. overnight to give 20% I (A = 2-pyridyl) (II). II and I
 (A = 4-pyridyl) enhanced the transcriptional activity of human
 PPAR. α . in
 CHO cells with EC50 of 0.353 and 0.235 μ M, resp., and that of
 human
 PPAR. γ . with EC50 of 0.30 and 0.14 μ M, resp.
 REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE
 FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

Divisional?

NO *NO*

L12 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001152658 CAPLUS

DOCUMENT NUMBER: 134:193426

TITLE: Preparation of substituted benzylthiazolidine-2,4-dione derivatives as agonists for peroxisomal

INVENTOR(S): proliferator activated receptor (PPAR) Miyachi, Hiroyuki; Nomura, Masahiro; Tanase, Takahiro;

PATENT ASSIGNEE(S): Murakami, Koji; Tsunoda, Masaki Kyorin Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 49 pp.

CODEN: PIXXDZ

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

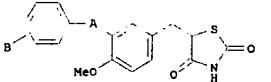
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014349	A1	20010301	WO 2000-JP5519	20000818
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG EP 1213287	A1	20020612	EP 2000-953475	20000818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			JP 1999-235527	A 19990823
PRIORITY APPLN. INFO.:			JP 2000-242706	A 20000810
			WO 2000-JP5519	W 20000818

OTHER SOURCE(S): MARPAT 134:193426

GI



L12 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2002 ACS (Continued)

AB The title compds. (I) or pharmaceutically acceptable salts thereof, or

hydrates of both (wherein A is CH_2CONH , NHCONH , $\text{CH}_2\text{CH}_2\text{CO}$, or NHCOCH_2 ; B is $\text{Cl}-1$ lower alkyl, $\text{Cl}-3$ lower alkoxy, halogeno, trifluoromethyl, trifluoromethoxy, substituted or unsubstituted Ph, substituted or unsubstituted phenoxy, or substituted or unsubstituted benzyloxy)

are prepd. These compds. bind as ligands to human peroxisome proliferator-activated receptor (PPAR) to thereby activate the receptor and exert antihyperglycemic and antihyperlipidemic effects. Thus,

378 mg 5-[(3-amino-4-methoxyphenyl)methyl]thiazolidine-2,4-dione was mixed with 5 mL THF, followed by adding 0.236 mL 4-trifluoromethyl isocyanate with stirring at room temp., and the stirring was continued at room temp. for 6 h, and left to stand overnight to give 5% 5-[(4-methoxy-3-[4-(trifluoromethyl)phenyl]ureidolphenyl)methyl]thiazolidine-2,4-dione (II).

II showed the transcription-activating activity for human PPAR. α . and PPAR. γ . in CHO cells with EC₅₀ of 0.55 and 0.43 μM , resp.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

=> S (E2 OR E3 OR E4) AND (PPAR?)
 172 "MURAKAMI KOICHI"/AU
 239 "MURAKAMI KOJI"/AU
 1 "MURAKAMI KOJIMA MASAYA"/AU
 2767 PPAR?
L13 21 ("MURAKAMI KOICHI"/AU OR "MURAKAMI KOJI"/AU OR "MURAKAMI
KOJIMA
 MASAYA"/AU) AND (PPAR?)

=> E TSUNODA MASAKI/AU 25
E1 2 TSUNODA MASAICHI/AU
E2 1 TSUNODA MASAICHTS/AU
E3 15 --> TSUNODA MASAKI/AU
E4 30 TSUNODA MASAKIYO/AU
E5 1 TSUNODA MASAKO/AU
E6 1 TSUNODA MASAKYO/AU
E7 16 TSUNODA MASAMI/AU
E8 2 TSUNODA MASANAO/AU
E9 1 TSUNODA MASANARI/AU
E10 13 TSUNODA MASAO/AU
E11 51 TSUNODA MASARU/AU
E12 13 TSUNODA MASASHI/AU
E13 6 TSUNODA MASATAKE/AU
E14 2 TSUNODA MASATO/AU
E15 1 TSUNODA MASATOSHI/AU
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E20 13 TSUNODA MAYUMI/AU
E21 1 TSUNODA MEGUMI/AU
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E23 1 TSUNODA MICHIHIKO/AU
E24 1 TSUNODA MIKI/AU
E25 7 TSUNODA MIKIO/AU

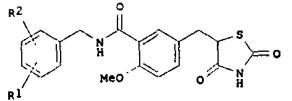
=> S (E3 OR E4) AND (PPAR?)
 15 "TSUNODA MASAKI"/AU
 30 "TSUNODA MASAKIYO"/AU
 2767 PPAR?
L14 6 ("TSUNODA MASAKI"/AU OR "TSUNODA MASAKIYO"/AU) AND (PPAR?)

=> DIS L14 1 IBIB ABS
THE ESTIMATED COST FOR THIS REQUEST IS 2.29 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L14 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:900080 CAPLUS
DOCUMENT NUMBER: 136:318816
TITLE: Design, synthesis and evaluation of substituted
phenylpropanoic acid derivatives as peroxisome
proliferator-activated receptor (PPAR)
activators: novel human PPAR
.alpha.-selective activators
AUTHOR(S): Miyachi, Hiroaki; Nomura, Masahiro; Tanase,
Takahiro;
Takehashi, Yukie; Ide, Tomohiro; Tsunoda,
Masaki; Murakami, Koji; Awano, Katsuya
CORPORATE SOURCE: Kyorin Pharmaceutical Co., Ltd., Discovery
Research
Laboratories, Tochigi, Shimotsuga-gun,
Nogi-machi,
329-0114, Japan
SOURCE: Bioorganic & Medicinal Chemistry Letters
(2001),
Volume Date 2002, 12(1), 77-80
CODEN: BMCLB8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB A series of substituted phenylpropanoic acid derivs. was prep'd. as
part of
a search for subtype-selective human peroxisome
proliferator-activated
receptor (PPAR) activators. Structure-activity relationship
studies indicated that the substituent at the .alpha.-position of
the carboxyl group plays a key role in detg. the potency and the
selectivity
for PPAR transactivation.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE
FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE
RE FORMAT

L14 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:152661 CAPLUS
 DOCUMENT NUMBER: 134:193428
 TITLE: Preparation of substituted
 benzylthiazolidine-2,4-dione derivatives as agonists of human
 peroxisome proliferator-activated receptor
 INVENTOR(S): Nomura, Masahiro; Murakami, Koji; Tsunoda,
 Mamaki; Takahashi, Yukie
 PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 19 pp.
 CODEN: PIIXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:
 PATENT NO. KIND DATE APPLICATION NO. DATE
 WO 2001014352 A1 20010301 WO 2000-JP5522 20000818
 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN,
 CR, CU,
 CZ, DE, DK, DN, ES, FI, GB, GD, GE, GH, GM, HR, HU,
 ID, IL,
 IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
 LV, MD,
 MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG,
 SI, SK,
 SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM,
 AZ, BY,
 KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE,
 CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE,
 BF, BJ,
 CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 EP 1207158 A1 20020522 EP 2000-953478 20000818
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE,
 MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL
 PRIORITY APPLN. INFO.: JP 1999-235530 A 19990823
 WO 2000-JP5522 W 20000818
 OTHER SOURCE(S): MARPAT 134:193428
 GI

3-01-2001
bad date

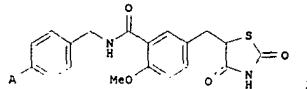


L14 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2002 ACS (Continued)
 AB The title compds. (I), pharmaceutically acceptable salts thereof
 and
 hydrates of the same (wherein R1 represents chloro, bromo, nitro,
 trifluoromethoxy, ethoxy, propoxy or isopropoxy; and R2 represents
 hydrogen or chloro) are prep'd. These compds. are capable of, as a
 ligand
 of human peroxisome proliferator-activated receptor (PPAR),
 enhancing the transcriptional activity of the receptor and showing
 effects
 of lowering blood sugar level and lowering lipid level; and a
 process for
 producing the same. Thus, 5-[(2,4-dioxothiazolidin-5-yl)methyl]-2-
 methoxybenzoic acid, Et3N, and CH2Cl2 were mixed, treated with Et
 chlorocarbonate and stirred under ice-cooling for 10 min, treated
 with
 4-nitrobenzylamine, and then stirred at room temp. for 2 h to give
 75%
 N-[(4-nitrophenyl)methyl]-5-[(2,4-dioxothiazolidin-5-yl)methyl]-2-
 methoxybenzamide (II). II and I (R1 = 4-n-Pro, R2 = H) enhanced
 the
 transcriptional activity of human PPAR α . in CHO cells with
 EC50 of 0.53 and 0.11 μ M, resp.
 REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE
 FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L14 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:152660 CAPLUS
 DOCUMENT NUMBER: 134:193427
 TITLE: Preparation of substituted
 benzylthiazolidine-2,4-
 peroxisome dione derivatives as agonists of human
 INVENTOR(S): Miyachi, Hiroyuki; Nomura, Masahiro; Tanase,
 Takahiro;
 PATENT ASSIGNEE(S): Murakami, Koji; Tsunoda, Masaki
 Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 20 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014351	A1	20010301	WO 2000-JP5521	20000818
W: AE, AL, AM, AT, AU, AZ, BA, BE, BG, BR, BY, CA, CH, CN, CR, CU, ID, IL, LV, MD, SI, SK,	CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LM, LR, LS, LT, LU, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1207157	A1	20020522	EP 2000-953477	20000818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
PRIORITY APPLN. INFO.:			JP 1999-235529 A 19990823	
			JP 2000-242707 A 20000810	
			WO 2000-JP5521 W 20000818	

OTHER SOURCE(S): MARPAT 134:193427
 GI

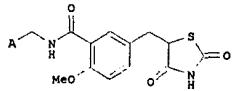


L14 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2002 ACS (Continued)
 AB The title compds. represented by general formula (I): wherein A
 represents
 optionally substituted Ph, optionally substituted phenoxy or
 optionally
 substituted benzyloxy), pharmaceutically acceptable salts thereof
 and
 hydrates of the same are prepd. These compds. are capable of, as
 a ligand
 of human peroxisome proliferator-activated receptor (PPAR),
 enhancing the transcriptional activity of the receptor and showing
 effects
 of lowering blood sugar level and lowering lipid level. Thus,
 5-[(2,4-dioxothiazolidin-5-yl)methyl]-2-methoxybenzoic acid, Et3N,
 and
 CH2Cl2 were mixed, treated with Et chlorocarbonate under
 ice-cooling, and
 stirred for 10 min under ice-cooling, followed by adding a soln. of
 4-benzyloxybenzylamine in CH2Cl2, and the resulting mixt. was
 stirred at
 room temp. for 2 h to give 7%
 N-[(4-benzyloxyphenyl)methyl]-5-[(2,4-
 dioxothiazolidin-5-yl)methyl]-2-methoxybenzamide (II). II and I
 (A = Ph)
 enhanced the transcriptional activity of human PPAR. α . in
 CHO cells with EC50 of 0.44 and 0.24 μ M, resp.
 REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE
 FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L14 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001152659 CAPLUS
 DOCUMENT NUMBER: 134:178551
 TITLE: Preparation of substituted
 benzylthiazolidine-2,4-dione derivatives as ligands of human
 peroxisome proliferator-activated receptor
 INVENTOR(S): Fujimori, Shizuo; Murakami, Koji; Tsunoda,
 Masaki
 PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 18 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014350	A1	20010301	WO 2000/JP5520	20000818
W:	AE, AL, AM, AR, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DR, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LCA, LR, LS, LT, LU, LV, MD, MG, MK, MN, MM, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TH RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG EP 1207156		EP 20020522	EP 2000-953476 20000818
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			
PRIORITY APPLN. INFO.:		JP 1999-235528	A 19990823	
		WO 2000-JP5520	W 20000818	

GI



AB The title compds. (I; wherein A represents pyridyl or cyclohexyl), pharmaceutically acceptable salts thereof and hydrates of the same are

L14 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2002 ACS (Continued)
 peroxisome proliferator-activated receptor (PPAR), enhancing the transcriptional activity of the receptor and showing effects of lowering blood sugar level and lowering lipid level. Thus, 5-[(2,4-dioxothiazolidin-5-yl)methyl]-2-methoxybenzoic acid, 2-picollylamine, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, and DMF were stirred at room temp. overnight to give 20% I (A = 2-pyridyl) (II). II and I (A = 4-pyridyl) enhanced the transcriptional activity of human PPAR α . in CHO cells with EC50 of 0.353 and 0.235 μ M, resp., and that of human PPAR γ . with EC50 of 0.30 and 0.14 μ M, resp.

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

ACCESSION NUMBER: 2001:152658 CAPLUS

DOCUMENT NUMBER: 134:193426

TITLE: Preparation of substituted

benzylthiazolidine-2,4-

dione derivatives as agonists for peroxisomal
proliferator activated receptor (PPAR)INVENTOR(S): Miyachi, Hiroyuki; Nomura, Masahiro; Tanase,
Takahiro;PATENT ASSIGNEE(S): Murakami, Koji; Tsunoda, Masaki
Kyorin Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 49 pp.

CODEN: PIKKD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

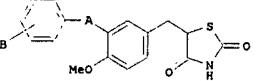
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014349	A1	20010301	WO 2000-JP5519	20000818
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, ID, IL, LV, MD, SI, SK, AZ, BY,	C2, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
EP 1213287	A1	20020612	EP 2000-953475	20000818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
PRIORITY APPLN. INFO.:			JP 1999-235527 A 19990823	
			JP 2000-242706 A 20000810	
			WO 2000-JP5519 W 20000818	

OTHER SOURCE(S): MARPAT 134:193426

GI



AB The title compds. (I) or pharmaceutically acceptable salts

thereof, or
hydrates of both (wherein A is CH₂CONH, NHCONN, CH₂CH₂CO, or
NHCOCH₂; B isC1-4 lower alkyl, C1-3 lower alkoxy, halogeno, trifluoromethyl,
trifluoromethoxy, substituted or unsubstituted Ph, substituted or
unsubstituted phenoxy, or substituted or unsubstituted benzyloxy)
are

are prep'd. These compds. bind as ligands to human peroxisome

proliferator-activated receptor (PPAR) to thereby activate the
receptor and exert antihyperglycemic and antihyperlipidemic

effects.

Thus, 378 mg

5-((3-amino-4-methoxyphenyl)methylthiazolidine-2,4-dione was

mixed with 5 mL THF, followed by adding 0.236 mL 4-trifluoromethyl

isocyanate with stirring at room temp., and the stirring was

continued at room temp. for 6 h, and left to stand overnight to give 57%

5-((4-methoxy-3-[3-[(4-(trifluoromethyl)phenyl)ureido]phenyl)methylthiaz

ol idine-2,4-dione (II). II showed the transcription-activating

activity for human PPAR_{alpha} and PPAR_{gamma} in CHO cells withEC₅₀ of 0.55 and 0.43 μM, resp.

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE

FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE

RE FORMAT

DOCUMENT NUMBER: 134:29211

TITLE: Preparation of phenylimethylcarbamoylphenylpropionic acid derivatives as human peroxisome proliferator-activated receptor- α . (PPAR- α) agonists

INVENTOR(S): Nomura, Masahiro; Takahashi, Yukie; Tanase,

Takahiro; Miyachi, Hiroyuki; Tsumoda, Masaki; Ide,

Tomohiro; Murakami, Koji Kyorin Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 90 pp.

CODEN: PIXDZ

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

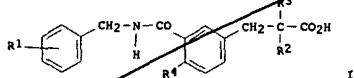
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000075103	A1	20001214	WO 2000-JP3707	20000608
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
JP 2001055367	A2	20010227	JP 2000-157600	20000529
BR 2000011734	A	20020305	BR 2000-11734	20000608
EP 1184366	A1	20020306	EP 2000-935582	20000608
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001006001	A	20020211	NO 2001-6001	20011207
PRIORITY APPLN. INFO.: JP 1999-162235	A	19990609		
JP 2000-157600	A	20000529		
WO 2000-JP3707	W	20000608		

OTHER SOURCE(S): MARPAT 134:29211

GI



AB The title compds. I [R1 = alkyl, etc.; R2 = alkyl, alkoxy, etc.; when R2 is alkyl, 2,2,2-trifluoroethyl, R3 is H, alkyl; when R2 is alkoxy, phenoxy, etc., R3 is H; R4 = alkoxy] are prep'd. I activate the PPAR- α receptors and lower blood lipid (cholesterol and neutral lipid) levels. 2-Ethyl-3-[4-methoxy-3-[N-(4-(trifluoromethyl)phenyl)methyl]carbamoyl]phenylpropionic acid at 30 mg/kg gave 55% decrease in total cholesterol in rats.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

12-14-2000

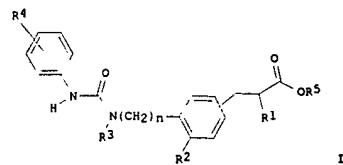
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E1 30 TAKAHASHI YUKI/AU
E2 1 TAKAHASHI YUKIBUMI/AU
E3 38 --> TAKAHASHI YUKIE/AU
E4 2 TAKAHASHI YUKIHARU/AU
E5 11 TAKAHASHI YUKIHIKO/AU
E6 92 TAKAHASHI YUKIHIRO/AU
E7 22 TAKAHASHI YUKIHISA/AU
E8 26 TAKAHASHI YUKIKO/AU
E9 26 TAKAHASHI YUKIMI/AU
E10 12 TAKAHASHI YUKINOBU/AU
E11 41 TAKAHASHI YUKINORI/AU
E12 324 TAKAHASHI YUKIO/AU
E13 2 TAKAHASHI YUKISHIGE/AU
E14 1 TAKAHASHI YUKISUKE/AU
E15 1 TAKAHASHI YUKITATSU/AU
E16 1 TAKAHASHI YUKITOMO/AU
E17 13 TAKAHASHI YUKITOSHI/AU
E18 31 TAKAHASHI YUKITSUGU/AU
E19 1 TAKAHASHI YUKIYO/AU
E20 1 TAKAHASHI YUKIYOSHI/AU
E21 60 TAKAHASHI YUKO/AU
E22 14 TAKAHASHI YUKOH/AU
E23 15 TAKAHASHI YUMI/AU
E24 1 TAKAHASHI YUMIE/AU
E25 1 TAKAHASHI YUMIHIRO/AU

=> S (E1 OR E2 OR E3) AND (PPAR?)
30 "TAKAHASHI YUKI"/AU
1 "TAKAHASHI YUKIBUMI"/AU
38 "TAKAHASHI YUKIE"/AU
2767 PPAR?
L15 6 ("TAKAHASHI YUKI"/AU OR "TAKAHASHI YUKIBUMI"/AU OR "TAKAHASHI YUKIE"/AU) AND (PPAR?)

=> DIS L15 1 IBIB ABS
THE ESTIMATED COST FOR THIS REQUEST IS 2.29 U.S. DOLLARS
DO YOU WANT TO CONTINUE WITH THIS REQUEST? (Y)/N:Y

L15 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2002:449639 CAPLUS
 DOCUMENT NUMBER: 137:33138
 TITLE: Preparation of ureidophenylalkanoic acid and ureidoalkylphenylalkanoic acid derivatives as peroxisome proliferator-activated receptor .alpha. (PPAR.alpha.) agonists
 INVENTOR(S): Miyachi, Hiroyuki; Takahashi, Yukie; Murakami, Kouji
 PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 35 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002046146	A1	20020613	WO 2001-JP10563	20011204
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GG, GW, ML, MR, NE, SN, TD, TG	JP 2000-369371 A 20001205	
PRIORITY APPLN. INFO.:	MARPAT 137:33138			
OTHER SOURCE(S): GI				



L15 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2002 ACS (Continued)

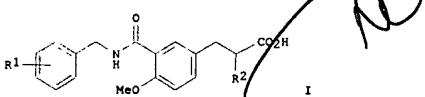
AB The title compds. I [R1, R3 and R5 represent each hydrogen or lower alkyl; R2 represents hydrogen or lower alkoxy; R4 represents hydrogen, trifluoromethyl, lower alkoxy, halogeno, optionally substituted phenoxy or benzyloxy; n is an integer of from 0 to 3; and the carboxylate substituent is located at the para-position relative to R2 or at the para-position relative to (CH₂)_n, useful as PPAR.alpha. agonists (no data), are prepd. I are useful in the treatment of diabetes, hyperlipidemia, obesity, and arteriosclerosis (no data). For example,

2-[(3-[4-(trifluoromethyl)phenyl]ureido)-4-methoxyphenyl]methyl]butyric acid was prepd.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2002428059 CAPLUS
 DOCUMENT NUMBER: 137:5998
 TITLE: Preparation of (phenylmethyl)alkanoic acid derivatives
 INVENTOR(S): Miyachi, Hiroyuki; Nomura, Masahiro; Takahashi, Rukie; Tanase, Takahiro; Murakami, Kouji
 PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 52 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002044130	A1	20020606	WO 2001-JP10353	20011128
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM		RW: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG		
PRIORITY APPLN. INFO.:	JP 2000-363677	A 20001129	OTHER SOURCE(S): MARPAT 137:5998	GI



AB The title compds. I (R1 represents hydrogen, halogeno, hydroxy, 2-phenylethyl, 2-phenylethoxy, hydroxyphenoxy or benzyloxyphenoxy; and R2 represents lower (C1-4) alkyl) are prep'd. I are lipid-lowering drugs

L15 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2002 ACS (Continued)
 (particularly in the liver), drugs preventing the progress of arteriosclerosis, anti-obesity drugs and remedies for diabetes.
 For example, 2-[(3-{(4-chlorophenyl)methyl}carbamoyl)-4-methoxyphenyl]methylbutyric acid (II) was prep'd. The PPAR alpha agonist activity of II was demonstrated.
 REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

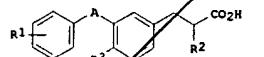
L15 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:900080 CAPLUS
DOCUMENT NUMBER: 136:318816
TITLE: Design, synthesis and evaluation of substituted phenylpropanoic acid derivatives as peroxisome proliferator-activated receptor (PPAR) activators: novel human PPAR α -selective activators
AUTHOR(S): Miyachi, Hiroyuki; Nomura, Masahiro; Tanase, Takahiro;
Takahashi, Yukie; Ide, Tomohiro; Tsunoda, Masaki; Murakami, Koji; Awano, Katuya
CORPORATE SOURCE: Kyorin Pharmaceutical Co., Ltd., Discovery Research
Laboratories, Tochigi, Shimotsuga-gun, Nogi-machi,
SOURCE: 329-0114, Japan
(2001), Bioorganic & Medicinal Chemistry Letters
Volume Date 2002, 12(1), 77-80
PUBLISHER: CODEN: BMCLB8; ISSN: 0960-894X
DOCUMENT TYPE: Elsevier Science Ltd.
LANGUAGE: Journal English
AB A series of substituted phenylpropanoic acid derivs. was prep'd. as part of a search for subtype-selective human peroxisome proliferator-activated receptor (PPAR) activators. Structure-activity relationship studies indicated that the substituent at the α -position of the carboxyl group plays a key role in detg. the potency and the selectivity for PPAR transactivation.
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

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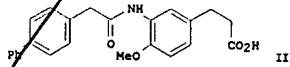
L15 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001886030 CAPLUS
 DOCUMENT NUMBER: 136:19941
 TITLE: Preparation of phenylpropionic acid
 derivatives as
 PPAR.alpha. activators effective as
 antiarteriosclerotics
 INVENTOR(S): Miyachi, Hiroyuki; Nomura, Masahiro; Takahashi,
 Yukie; Tanase, Takahiro; Murakami, Kouji;
 Suzuki,
 Masahiro
 Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 115 pp.
 CODEN: PIKXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:
 12.00.01

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001052201	A1	20011206	WO 2001-JP4385	20010525
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.: JP 2000-158424			A 20000529	
OTHER SOURCE(S): MARPAT 136:19941				
G1				

L15 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2002 ACS (Continued)



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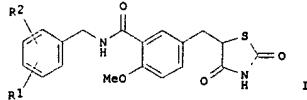


II

AB Title compds. [I; R1 = alkyl, alkoxy, trifluoromethyl, trifluoromethoxy, Ph, phenoxy, benzyloxy; R2 = H, alkyl, alkoxy; R3 = alkoxy; A = CH2CONH, NHCOCH2, CH2CH2CO, CH2CH2CH2, CH2CH2O, CONHCH2, CH2NHCH2, COCH2O, OCH2CO, COCH2NH, NHCH2CO], stereoisomers, and pharmaceutically acceptable salts, which bind to human peroxisome proliferator activated receptor .alpha. (PPAR.alpha.) as ligand to activate the receptor and thereby exhibit a potent lipid-decreasing effect, are prepd. as antiarteriosclerotics. Thus, the title compd. II was prepd. and biol. tested for transcription activation effect with EC50(.mu.mol/L) = 0.05.
 REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001152661 CAPLUS
 DOCUMENT NUMBER: 134:193428
 TITLE: Preparation of substituted
 benzylthiazolidine-2,4-
 peroxisome dione derivatives as agonists of human
 INVENTOR(S): Nomura, Masahiro; Murakami, Koji; Tsunoda,
 Masaaki;
 PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 19 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014352	A1	20010301	WO 2000-JP5522	20000818
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG EP 1207158	A1	20020522	EP 2000-953478	20000818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			JP 1999-235530	A 19990823
PRIORITY APPLN. INFO.:			WO 2000-JP5522	W 20000818
OTHER SOURCE(S):	MARPAT 134:193428			
GI				



L15 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2002 ACS (Continued)
 AB The title compds. (I), pharmaceutically acceptable salts thereof
 and hydrates of the same (wherein R1 represents chloro, bromo, nitro,
 trifluoromethoxy, ethoxy, propoxy or isopropoxy; and R2 represents
 hydrogen or chloro) are prep'd. These compds. are capable of, as a
 ligand of human peroxisome proliferator-activated receptor (PPAR),
 enhancing the transcriptional activity of the receptor and showing
 effects of lowering blood sugar level and lowering lipid level; and a
 process for
 producing the same. Thus, 5-[(2,4-dioxothiazolidin-5-yl)methyl]-2-
 methoxybenzoic acid, Et₃N, and CH₂C₁₂ were mixed, treated with Et
 Chlorocarbonate and stirred under ice-cooling for 10 min, treated
 with 4-nitrobenzylamine, and then stirred at room temp. for 2 h to give
 751 N-[(4-nitrophenyl)methyl]-5-[(2,4-dioxothiazolidin-5-yl)methyl]-2-
 methoxybenzamide (II). II and I (R1 = 4-n-Pro, R2 = H) enhanced
 the transcriptional activity of human PPAR. α . in CHO cells with
 EC₅₀ of 0.53 and 0.11 μ M, resp.
 REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE
 FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L15 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:881114 CAPLUS
 DOCUMENT NUMBER: 134:29211
 TITLE: Preparation of
 phenylimethylcarbamoylphenylpropionic
 acid derivatives as human peroxisome
 proliferator-activated receptor-.alpha. (PPAR
 -alpha.) agonists
 INVENTOR(S): Nomura, Masahiro; Takahashi, Yukie; Tanase,
 Takahiro; Miyachi, Hiroyuki; Tsunoda, Masaki;

Ide,

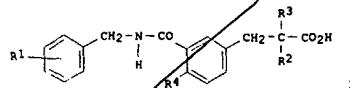
PATENT ASSIGNEE(S): Tomohiro; Murakami, Koji
 Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 90 pp.
 CODEN: PIXKD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000075103	A1	20001214	WO 2000-JP3707	20000608
	W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, ID, IL, MD, MG, SK, SL, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, BF, BJ, MC, PT, IE, SI, LT, LV, FI, RO NO 200106001 A 20020211		
			JP 2000-157600	20000529
PRIORITY APPN. INFO.:			BR 2000011734 A 20020305	20000608
			EP 1184366 A1 20020306	20000608
			R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, NO 200106001 A 20010227	
			JP 1999-162235 A 19990609	
			JP 2000-157600 A 20000529	
			WO 2000-JP3707 W 20000608	

OTHER SOURCE(S): MARPAT 134:29211
 GI

L15 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2002 ACS (Continued)



AB The title compds. I [R1 = alkyl, etc.; R2 = alkyl, alkoxy, etc.; when R2 is alkyl, 2,2,2-trifluoroethyl, R3 is H, alkyl; when R2 is alkoxy, phenoxy, etc., R3 is H; R4 = alkoxy] are prep'd. I activate the PPAR-.alpha. receptors and lower blood lipid (cholesterol and neutral lipid) levels. 2-Ethyl-3-[4-methoxy-3-[N-[4-(trifluoromethyl)phenyl]methyl]carbamoylphenyl]propionic acid at 30 mg/kg gave 55% decrease in total cholesterol in rats.

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> fil caplus			
COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION	
FULL ESTIMATED COST	267.97	414.57	
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION	
CA SUBSCRIBER PRICE	-36.55	-36.55	

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 FILE LAST UPDATED: 11 Aug 2002 (20020811/ED)

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=> s PPAR?
L16      2767 PPAR?

=> s bezylthia?
L17      0 BEZYLTHIA?

=> s benzylthia?
L18      227 BENZYLTHIA?

=> s l16 and l18 ful
L19      5 L16 AND L18

=> d his
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(FILE 'HOME' ENTERED AT 09:59:58 ON 12 AUG 2002)

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FILE 'REGISTRY' ENTERED AT 10:01:05 ON 12 AUG 2002
L1      STRUCTURE uploaded
L2      46 S L1 FUL
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L3 46 S L2 AND CAPLUS/LC

FILE 'CAPLUS' ENTERED AT 10:04:24 ON 12 AUG 2002
L4 32 S L2 FUL
L5 990331 S BLOOD?
L6 12 S L4 AND L5
E NOMURA MASAHIRO/AU 25
L7 3 S (E2 OR E3 OR E4) AND (BENZYLTHIA?)
L8 11 S (E2 OR E3 OR E4) AND (LIPID?)
E MURAKAMI KOJI/AU 25
L9 17 S (E2 OR E3 OR E4) AND (LIPID?)
L10 0 S (E2 OR E3 OR E4) AND (BEZYLTHI?)
L11 0 S (E2 OR E3 OR E4) AND (BEZYLTHIAZ?)
L12 4 S (E2 OR E3 OR E4) AND (BENZYLTHI?)
L13 21 S (E2 OR E3 OR E4) AND (PPAR?)
E TSUNODA MASAKI/AU 25
L14 6 S (E3 OR E4) AND (PPAR?)
E TAKAHASHI YUKIE/AU 25
L15 6 S (E1 OR E2 OR E3) AND (PPAR?)

FILE 'CAPLUS' ENTERED AT 10:15:15 ON 12 AUG 2002
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L17 0 S BEZYLTHIA?
L18 227 S BENZYLTHIA?
L19 5 S L16 AND L18 FUL

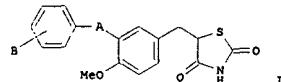
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L20 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:653768 CAPLUS
 DOCUMENT NUMBER: 136:47967
 TITLE: Interaction between peroxisome
 proliferator-activated receptor .gamma. and its agonists: docking
 study of oximes having 5-benzyl-2,4-thiazolidinedione
 AUTHOR(S): Iwata, Y.; Miyamoto, S.; Takamura, M.;
 Yanagisawa, H.; Kasuya, A.
 CORPORATE SOURCE: Exploratory Chemistry Research Laboratories,
 Sankyo Co., Ltd., Tokyo, Japan
 SOURCE: Journal of Molecular Graphics & Modelling
 (2001), 19(6), 536-542
 PUBLISHER: Elsevier Science Inc.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB The mol. modeling of oximes having 5-benzyl-2,4-thiazolidinedione
 moieties, agonists of the peroxisome proliferator-activated
 receptor .gamma. (PPAR.gamma.), was performed with respect to their
 structures complexed with the ligand binding domain of PPAR
 .gamma.. For each ligand mol., the 5-benzyl-2,4-thiazolidinedione
 head group was used as an anchor and the conformation of the rest of
 the mol. was searched for the most energetically favorable interaction with
 the receptor by systematic conformation search and manual modeling.
 Although both tail-up and tail-down configurations, which have been obstd.
 in the crystal structure of eicosapentaenoic acid when complexed with
 PPAR.delta., appeared among the lowest energy structures for most
 of the compds., potent agonists were found to adopt a configuration
 similar to that of rosiglitazone when bound to PPAR.gamma.,
 according to the crystal structure. The structure-activity
 relationships were analyzed based on the receptor-ligand interaction. The alkyl
 group and the arom. ring of the tail group of the ligands had hydrophobic
 interactions with the receptor, and these interactions were
 essential for the strong activity.
 REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L20 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:152658 CAPLUS
 DOCUMENT NUMBER: 134:193426
 TITLE: Preparation of substituted benzylthiazolidine
 -2,4-dione derivatives as agonists for
 peroxisomal proliferator activated receptor (PPAR)
 INVENTOR(S): Miyachi, Hiroyuki; Nomura, Masahiro; Tanase,
 Takahiro; Murakami, Koji; Tsunoda, Masaki
 PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 49 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:
 NO

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014349	A1	20010301	WO 2000-JP5519	20000818
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG EP 1213287	A1 20020612	EP 2000-953475 20000818		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL	JP 1999-235527	A 13990823		
PRIORITY APPLN. INFO.: JP 2000-242706	JP 2000-242706	A 13990810		
OTHER SOURCE(S): MARPAT 134:193426	WO 2000-JP5519	W 20000818		
GI				



L20 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2002 ACS (Continued)
 AB The title compds. (I) or pharmaceutically acceptable salts
 thereof, or
 hydrates of both (wherein A is CH₂CONH, NHCONH, CH₂CH₂CO, or
 NHOCH₂; B is
 Cl-4 lower alkyl, Cl-3 lower alkoxy, halogeno, trifluoromethyl,
 trifluoromethoxy, substituted or unsubstituted Ph, substituted or
 unsubstituted phenoxy, or substituted or unsubstituted benzyloxy)
 are
 prepd. These compds. bind as ligands to human peroxisome
 proliferator-activated receptor (PPAR) to thereby activate the
 receptor and exert antihyperglycemic and antihyperlipidemic
 effects.
 Thus, 378 mg
 5-[(3-amino-4-methoxyphenyl)methyl]thiazolidine-2,4-dione was
 mixed with 5 mL THF, followed by adding 0.236 mL 4-trifluoromethyl
 isocyanate with stirring at room temp., and the stirring was
 continued at room temp. for 6 h, and left to stand overnight to give 57%
 5-[(4-methoxy-3-(3-(4-(trifluoromethyl)phenyl)ureido)phenyl)methyl]thiazolidine-2,4-dione (II). II showed the transcription-activating
 activity for human PPAR.alpha. and PPAR.gamma. in CHO cells with
 EC₅₀ of 0.55 and 0.43 .mu.M resp.
 REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

Foreign priority document

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=> s dioxothia?
L21      247 DIOXOTHIA?

=> d his

(FILE 'HOME' ENTERED AT 09:59:58 ON 12 AUG 2002)

FILE 'REGISTRY' ENTERED AT 10:01:05 ON 12 AUG 2002
L1      STRUCTURE UPLOADED
L2      46 S L1 FUL
L3      46 S L2 AND CAPLUS/LC

FILE 'CAPLUS' ENTERED AT 10:04:24 ON 12 AUG 2002
L4      32 S L2 FUL
L5      990331 S BLOOD?
L6      12 S L4 AND L5
      E NOMURA MASAHIRO/AU 25
L7      3 S (E2 OR E3 OR E4) AND (BENZYLTHIA?)
L8      11 S (E2 OR E3 OR E4) AND (LIPID?)
      E MURAKAMI KOJI/AU 25
L9      17 S (E2 OR E3 OR E4) AND (LIPID?)
L10     0 S (E2 OR E3 OR E4) AND (BEZYLTHI?)
L11     0 S (E2 OR E3 OR E4) AND (BEZYLTHIAZ?)
L12     4 S (E2 OR E3 OR E4) AND (BENZYLTHI?)
L13     21 S (E2 OR E3 OR E4) AND (PPAR?)
      E TSUNODA MASAKI/AU 25
L14     6 S (E3 OR E4) AND (PPAR?)
      E TAKAHASHI YUKIE/AU 25
L15     6 S (E1 OR E2 OR E3) AND (PPAR?)

FILE 'CAPLUS' ENTERED AT 10:15:15 ON 12 AUG 2002
L16     2767 S PPAR?
L17     0 S BEZYLTHIA?
L18     227 S BENZYLTHIA?
L19     5 S L16 AND L18 FUL
L20     2 S L19 NOT L4
L21     247 S DIOXOTHIA?

=> s l21 and l16
L22      9 L21 AND L16

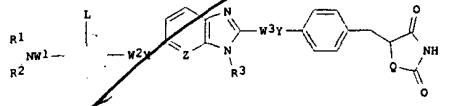
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L23      8 L22 NOT L20

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L24      5 L23 NOT L19

=> d l24 1-5 ibib abs hitstr
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L24 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2002:479961 CAPLUS
 DOCUMENT NUMBER: 137:41755
 TITLE: Antidiabetic agents containing amine
 derivatives
 and their
 having benzimidazole or imidazopyridine ring
 other uses
 INVENTOR(S): Fujita, Takashi; Wada, Kunio; Oguchi, Minoru;
 Honma,
 Sigeji; Fujiwara, Toshihiko
 PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 109 pp.
 CODEN: JKXKAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

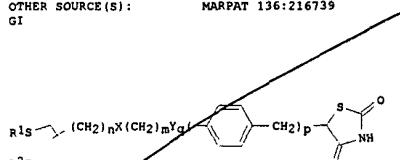
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2002179568	A2	20020626	JP 2001-308814	20011004
PRIORITY APPN. INFO.:			JP 2000-307159	A 20001006
OTHER SOURCE(S):	MARPAT 137:41755			



AB Prophylactic and/or therapeutic agents for diabetes, glucose intolerance, diabetic complications, or gestational diabetes contain the derivs. I (R1 = carbamoyl which may have 1-2 .alpha., thiocarbamoyl which may have 1-2 .alpha., sulfonyl having 1 .alpha., carbonyl having 1 .alpha.; R2, R3 = H, Cl-10 alkyl, C6-10 aryl, which may have 1-3 .beta., C7-16 aralkyl which may have 1-3 .beta. on the aryl moiety; W1-W3 = direct bond, Cl-8 alkylene; X, Y, Q = O, S; Z = :CH, N' Ar = benzene or naphthalene ring substituted with 1-4 L; L = H, Cl-6 alkyl, C6-10 aryl which may have 1-3 .beta., C7-16 aralkyl which may have 1-3 .beta. on the aryl moiety; definitions of .alpha. and .beta. are given) or their pharmol. acceptable salts. I and their salts are also useful as insulin resistance

L24 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2002:165043 CAPLUS
 DOCUMENT NUMBER: 136:216739
 TITLE: Preparation of dithiolanyl thiazolidinediones
 as peroxisome proliferator-activated receptor
 .gamma. activators.
 INVENTOR(S): Pershadisingh, Harrihar A.; Avery, Mitchell A.
 PATENT ASSIGNEE(S): University of Mississippi, USA
 SOURCE: U.S., 38 pp., Cont.-in-part of U. S. Ser. No. 6,204,288.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6353011	B1	20020305	US 2000-520208	20000307
US 6127394	A	20001003	US 1999-264370	19990308
US 6204288	B1	20010320	US 2000-497324	20000203
PRIORITY APPN. INFO.:			US 1999-264370	A2 19990308
OTHER SOURCE(S):	MARPAT 136:216739		US 2000-497324	A2 20000203



AB Title compds. [I; R1 R2 = H, COR6 CSR6; R6 = H, alkyl, aryl, aralkyl, carboxy, NR7R8, OR7, NHR7, SR7, NR7R8; R7, R8 = H, alkyl, aryl, aralkyl; R1R2 = atoms to form a 1,2-dithiolane ring; X = O, NR, CO2, OCOC2, CONR; R = H, (substituted) alkyl, aryl; Y = O, S, NR3; R3 = H, (substituted) alkyl; n = 2-14; m = 0-14; q, t = 0, 1; when m = 0 then q = 0], were prep'd. as peroxisome proliferator-activated receptor .gamma. activators (no data). Thus, 5-[4-(2-aminoethoxy)phenyl]methyl]-1,3-thiazolidine-2,4-dione hydrochloride at CH2Cl2 at 0.degree. was treated with Et3N and then with a mixt. prep'd. from DL-lipoic acid, Et3N, and iso-Pr chloroformate in

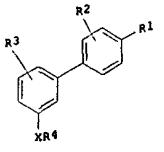
L24 ANSWER 1 OF 5 CAPLUS COPYRIGHT 2002 ACS (Continued)
 improving agents, hypoglycemics, inflammation inhibitors, immunomodulators, aldose reductase inhibitors, 5-lipoxygenase inhibitors, lipid peroxide formation inhibitors, PPAR activators, antiosteoporotic agents, leukotriene antagonists, adipocyte conversion promoters, cancer cell growth inhibitors, and Ca blockers. Feeding diabetic KK mice with feed contg. 0.01% 1-(4-chlorophenyl)-3-[4-[2-[4-(2,4-dioxothiazolidin-5-ylmethyl)phenoxy)methyl]-1-methyl-1H-benzimidazol-6-yloxy]-2,6-dimethylphenyl)thiourea (II) for 3 days showed 48.9% hypoglycemic effect. Capsules, tablets, and granules contg. II were also formulated.

L24 ANSWER 2 OF 5 CAPLUS COPYRIGHT 2002 ACS (Continued)
 toluene/CH2Cl2 followed by stirring to give 56% N-[2-[4-[2,4-dioxo-1,3-thiazolidin-5-yl]methyl]phenoxy]ethyl]-5-(1,2-dithiolan-3-yl)pentanamide
 REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

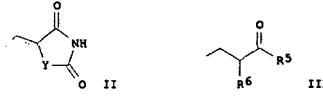
L24 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2002:122976 CAPLUS
 DOCUMENT NUMBER: 136:167181
 TITLE: Preparation of biphenyl derivatives and their
 use as
 INVENTOR(S): PPAR gamma receptor agonists
 Bernardon, Jean-Michel; Clary, Laurence
 PATENT ASSIGNEE(S): Galderma Research & Development, Fr.
 SOURCE: PCT Int. Appl., 113 pp.
 CODEN: PIXKD2
 DOCUMENT TYPE: Patent
 LANGUAGE: French
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002012210	A1	20020214	WO 20010803	20010803
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MM, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TS, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MM, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG FR 2812876	A1	20020215	FR 2000-10447	20000808
AU 2001085981	A5	20020218	AU 2001-85981	20010803
PRIORITY APPLN. INFO.:			FR 2000-10447	A 20000808
			WO 2001-FR2543	W 20010803
OTHER SOURCE(S):	MARPAT 136:167181			
GI				

L24 ANSWER 3 OF 5 CAPLUS COPYRIGHT 2002 ACS (Continued)



I

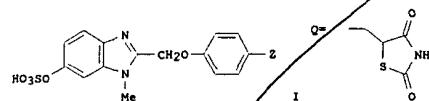


AB The invention concerns compds. I (e.g. N-[4'-(2,4-dioxothiazolidin-5-ylmethyl)biphenyl-3-yl]methyl-N-methylbenzamide) wherein: R1 represents a radical II or III; Y represents a CH2 radical or a S atom; R5 represents hydroxy, alkoxy, NH-OH, or N(R8)(R9) radical; and R6 represents alkyl, OR10, SR10, or (CH2)r-COR11. Said compds. are useful as PPAR gamma receptor activators in pharmaceutical compns. for use in human or veterinary medicine (in dermatol., as well as in the field of cardiovascular diseases, immune diseases and/or diseases related to lipid metab.), or in cosmetic compns. Agonist activity for 15 of the claimed compds. is reported. Although the methods of prepn. are not claimed, 82 example prepns. are included. REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L24 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:254872 CAPLUS
 DOCUMENT NUMBER: 134:280842
 TITLE: Preparation of 2-phenoxymethyl-1-methyl-6-sulfoxybenzimidazoles with blood sugar-lowering activity
 INVENTOR(S): Iwabuchi, Haruo; Fujiwara, Toshihiko; Fujita, Takashi
 PATENT ASSIGNEE(S): Sankyo Co., Ltd., Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 28 pp.
 CODEN: JKXKAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001097954	A2	20010410	JP 2000-228085	20000728
PRIORITY APPLN. INFO.:			JP 1999-215140	A 19990729
OTHER SOURCE(S):	MARPAT 134:280842			
GI				

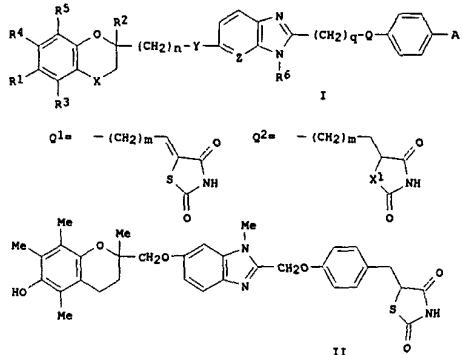
L24 ANSWER 4 OF 5 CAPLUS COPYRIGHT 2002 ACS (Continued)
 (prepns. given) in 100 mL pyridine over a period of 30 min and left to stand at room temp. for 18 h to give, after workup and reversed phase chromatog., 5-[4-(6-sulfoxy-1-methyl-1H-benzimidazol-2-ylmethoxy)benzyl]thiazolidine-2,4-dione (II). A dispersant, tablet, or capsule formulation contg. II was prep'd.



AB The title compds. [I; Z = Q, CH2CH(COY)S(O)nR; wherein Y = OH, NH2; R = C1-5 linear or branched alkyl; n = 0,1,2] are prep'd. These compds. also possess insulin-resistance improving, antiinflammatory, immunomodulating, aldose reductase-inhibitory, 5-lipoxygenase-inhibitory, lipid peroxide formation-inhibitory, peroxisome proliferator-activated receptor (PPAR)-activating, anti-osteoporosis, leukotriene antagonist, fat cellularization, cancer proliferation-inhibitory, or calcium antagonist activity and are useful for the prevention or treatment of diseases caused by insulin resistance, diabetes, hyperglycemia, diabetes complications, or cancer (no data). Thus, a soln. of 0.80 mL chlorosulfonic acid in 100 mL MeCN was added dropwise to a soln. of 3.36 g 5-[4-(6-hydroxy-1-methyl-1H-benzimidazol-2-ylmethoxy)benzyl]thiazolidine-2,4-dione hydrochloride

L24 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000742095 CAPLUS
 DOCUMENT NUMBER: 133:296438
 TITLE: Preparation of substituted fused imidazole derivatives
 INVENTOR(S): Fujita, Takashi; Wada, Kunio; Oguchi, Minoru; Honma,
 PATENT ASSIGNEE(S): Hidehito; Fujiwara, Toshihiko
 SANKYO COMPANY, Limited, Japan
 SOURCE: PCT Int. Appl., 274 pp.
 CODEN: PIWMD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:
 PATENT NO. KIND DATE APPLICATION NO. DATE
 WO 2000061582 A1 20001019 WO 2000-JP2217 20000406
 W: AU, BR, CA, CN, CZ, HU, ID, IL, IN, KR, MX, NO, NZ, PL,
 RU, TR,
 US, CA
 RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU,
 MC, NL,
 JP 200034777 A2 20001219 JP 2000-105985 20000407
 PRIORITY APPLN. INFO.: JP 1999-101369 A 19990408
 OTHER SOURCE(S): MARPAT 133:296438
 GI

L24 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2002 ACS (Continued)



AB Compds. represented by general formula (I) and salts and esters thereof
 [wherein R1 is hydrogen, Cl-6 alkyl, (un)substituted C6-10 aryl or C7-16 aralkyl, HO, (un)substituted acyloxy, Cl-6 alkoxy, (un)substituted NH2, etc.; R2 is hydrogen, Cl-6 alkyl, or (un)substituted C7-16 aralkyl; R4, R5 is each hydrogen, Cl-6 alkyl, or Cl-6 alkoxy; R6 is hydrogen, Cl-6 alkyl, (un)substituted C6-10 aryl or C7-16 aralkyl; Q and Y are each oxygen or sulfur; X is CH2, CO, CH(R9), or C(=O)R10; wherein R9 or R10 is hydrogen, (un)substituted Cl-6 alkyl, C7-16 aralkyl, or acyl; Z is CH or nitrogen; n and q are each 1 to 5; and A is a group represented by general formula Q1, Q2, Q3, or (CH2)2-CH(CO2H)-BR7; wherein m is 0 to 8; X1 is oxygen or sulfur; B is oxygen, sulfur, or (un)substituted NH; and R7 is hydrogen, Cl-6 alkyl, (un)substituted C6-10 aryl or C7-16 aralkyl, or haloalkyl] are prepd. These compds. are useful as insulin resistance

L24 ANSWER 5 OF 5 CAPLUS COPYRIGHT 2002 ACS (Continued)
 improvers, hypoglycemics, antiinflammatory agents, immunomodulators, aldose reductase inhibitors, 5-lipoxygenase inhibitors, lipid peroxide-formation inhibitors, peroxisome proliferator-activated receptor (PPAR) activators, anti-osteoporosis agents, leukotriene antagonists, promoters of fat cell formation, cancer cell-proliferation inhibitors, or calcium antagonists. They are useful for the prevention of treatment of diabetes, hyperlipidemia, obesity, glucose tolerance insufficiency, hypertension, fatty liver, diabetes complication, arteriosclerosis, gestational diabetes, polycystic ovarian syndrome, cardiovascular diseases, cell damages caused by atherosclerosis or ischemic heart diseases, gout, osteoarthritis, rheumatic arthritis, allergic diseases, asthma, gastrointestinal ulcer, cachexia, autoimmune diseases, cancer, osteoporosis, or cataract. Thus, N-[2-amino-5-(6-methoxymethoxy-2,5,7,8-tetramethylchroman-2-ylmethoxy)phenyl]-N-methylcarbamic acid tert-Bu ester was condensed with 4-[2,4-dioxothiazolin-5-ylmethyl]phenoxyacetic acid using di-Et cyanophosphate and Et3N in THF at room temp. for 30 min, followed by treatment of the product with 4 N HCl/dioxane at room temp. for 5 h gave 5-[4-[6-(6-hydroxy-2,5,7,8-tetramethylchroman-2-ylmethoxy)-1-methyl-1H-benzimidazol-2-ylmethoxy]benzyl]thiazolidine-2,4-dione hydrochloride (II.HCl). When a feed contg. 0.01% II.HCl was fed to mice for 3 days, the blood sugar level was lowered by 66.7% compared to control animal. REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	24.12	438.69
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-4.34	-40.89

STN INTERNATIONAL LOGOFF AT 10:17:52 ON 12 AUG 2002

FILE 'HOME' ENTERED AT 09:59:58 ON 12 AUG 2002

FILE 'REGISTRY' ENTERED AT 10:01:05 ON 12 AUG 2002
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DICTIONARY FILE UPDATES: 9 AUG 2002 HIGHEST RN 443534-23-4

TSCA INFORMATION NOW CURRENT THROUGH January 7, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

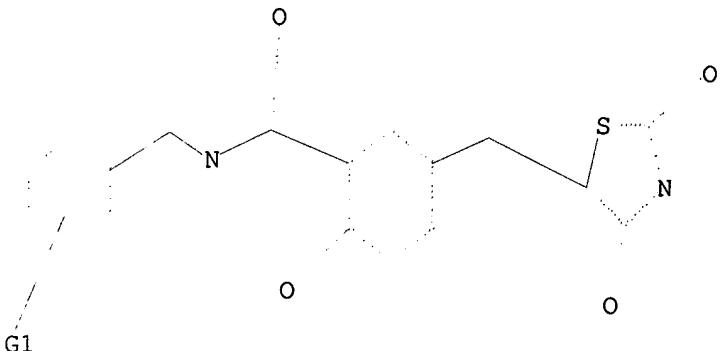
Crossover limits have been increased. See **HELP CROSSOVER** for details.

Calculated physical property data is now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

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L1 STRUCTURE UPLOADED

=> d
L1 HAS NO ANSWERS
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H 1 Cl 2
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Structure attributes must be viewed using STN Express query preparation.

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100.0% PROCESSED 108 ITERATIONS 46 ANSWERS
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      23846251 CAPLUS/LC
L3 46 L2 AND CAPLUS/LC
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FILE COVERS 1907 - 12 Aug 2002 VOL 137 ISS 7
FILE LAST UPDATED: 11 Aug 2002 (20020811/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

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L4 32 L2

=> s blood?
L5 990331 BLOOD?

=> s 14 and 15
L6 12 L4 AND L5

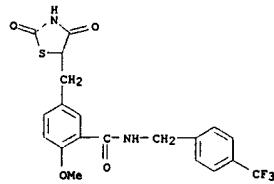
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L4 ANSWER 1 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 20021540258 CAPLUS
 TITLE: Preparation of benzoxepinopyridines as HMG-CoA
 reductase inhibitors
 INVENTOR(S): Robl, Jeffrey A.; Chen, Bang-chi; Sun,
 Chong-qing
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 42 pp., Cont.-in-part
 of U.S.
 Ser. No. 875,155.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002094977	A1	20020718	US 2001-7407	20011204
US 2002013334	A1	20020131	US 2001-875155	20010606
PRIORITY APPLN. INFO.:			US 2000-211595P P	20000615
			US 2001-875155	A2 20010606

GI

L4 ANSWER 1 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)



* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [X = O, S, SO₂, NR₇; Z = HOCH₂CH(OH)CH₂CO₂R₃, 4-hydroxy-2-oxopyran-6-yl, etc.; n = 0, 1; R₁, R₂ = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R₃ = H, alkyl, metal ion; R₄ = H, halo, CF₃, etc.; R₇ = H, alkyl, aryl, alkanoyl, acroyl, alkoxycarbonyl, etc.; R₉, R₁₀ = H, alkyl], were prepd. as HMG CoA reductase inhibitors active in inhibiting cholesterol biosynthesis, modulating blood serum lipids such as lowering LDL cholesterol and/or increasing HDL cholesterol, and treating hyperlipidemia, hypercholesterolemia, hypertriglyceridemia and atherosclerosis (no data). E.g., a multistep synthesis of II is reported.

IT 213252-19-8, KRP297

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (coadministered agents; prepn. of benzoxepinopyridines as

HMG-CoA reductase inhibitors for the treatment of hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, and other disorders)

RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]-(9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 20021504648 CAPLUS
 DOCUMENT NUMBER: 137:83637
 TITLE: Medicinal compositions containing diuretic and insulin
 resistance-improving agent
 INVENTOR(S): Takakura, Masaya; Araki, Kazushi; Kanda, Shoichi
 PATENT ASSIGNEE(S): Sankyo Company, Limited, Japan
 SOURCE: PCT Int. Appl., 183 PP.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002051441	A1	20020704	WO 2001-JP11296	20011221
W: AU, BR, CA, CN, CO, CZ, HU, ID, IL, IN, KR, MX, NO, NZ, PH, PL,				
RU, SG, SK, US, VN, 2A RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,				
PT, SE, TR				

PRIORITY APPLN. INFO.: JP 2000-394424 A 20001226
 OTHER SOURCE(S): MARPAT 137:83637

AB Disclosed are medicinal compns. contg. a diuretic and an insulin resistance-improving agent whereby side effects assocg. the administration of an insulin resistance-improving agent (for example, megalocardia, edema, body fluid retention, pleural effusion) can be prevented or treated. Oral administration of furosemide prevented increases of heart wt. and blood plasma, and edema due to administration of

5-[4-(6-methoxy-1-methyl-1H-benzimidazol-2-ylmethoxy)benzyl]thiazolidine

-2,4-dione hydrochloride.

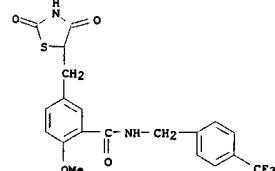
IT 213252-19-8, KRP-297

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (medicinal compns. contg. diuretics and insulin resistance-improving agents)

RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]-(9CI) (CA INDEX NAME)

L4 ANSWER 2 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L4 ANSWER 3 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2002:409256 CAPLUS
 DOCUMENT NUMBER: 137:735
 TITLE: Methods and compositions for treatment of diabetes and related conditions via gene therapy
 INVENTOR(S): Caplan, Shari L.; Boettcher, Brian R.; Slosberg, Eric D.; Connally, Sheila; Kaleko, Michael; Desai, Urvi J.
 PATENT ASSIGNEE(S): USA U.S. Pat. Appl. Publ., 42 pp.
 SOURCE: CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

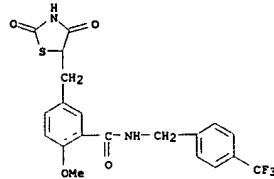
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002065239	A1	20020530	US 2001-808457	20010314

PRIORITY APPLN. INFO.: US 2000-266328P P 20000315
 AB Methods and compns. are disclosed for the treatment of diabetes, obesity and diabetic-related conditions. The methods include gene therapy based administration of a therapeutically effective amt. of vectors encoding the following: glucokinase regulatory protein alone or co-administered with glucokinase or with metab. modifying proteins; glucokinase co-administered with metab. modifying proteins; or glucokinase regulatory protein co-administered with glucokinase in combination with metab. modifying proteins, to a diabetic patient. The metab. modifying proteins include UCP2, UCP3, PPAR.alpha., OB-Rb, GLP-1 and GLP-1 analogs (administered via vector or directly as a peptide). Preferred examples of GLP-1 analogs include GLP-1-Gly8, Exendin-4 and the "Black Widow" chimeric GLP-1 analog. Addnl., PPAR.alpha. ligands and DPP-IV inhibitors may be co-administered with the above.

IT 213252-19-8, KRP-297
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (gene therapy for treatment of diabetes and related conditions)

RN 213252-19-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)

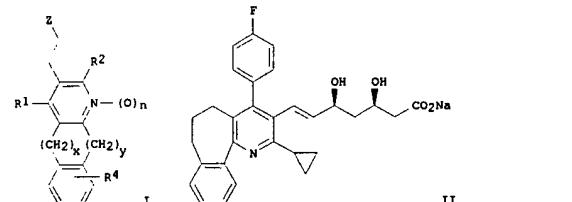
L4 ANSWER 3 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)



L4 ANSWER 4 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2002:392237 CAPLUS
 DOCUMENT NUMBER: 136:401651
 TITLE: Preparation of fused pyridine derivatives as HMG-CoA reductase inhibitors
 INVENTOR(S): Robl, Jeffrey A.; Chen, Bang-Chi; Sun, Chong-Qing
 PATENT ASSIGNEE(S): USA U.S. Pat. Appl. Publ., 46 pp., Cont.-in-part of U.S.
 SOURCE: Ser. No. 875,218.
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

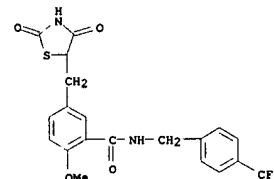
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002061901	A1	20020523	US 2001-8154	20011204
US 2002028826	A1	20020307	US 2001-875218	20010606

PRIORITY APPLN. INFO.: US 2000-211594P P 20000615
 OTHER SOURCE(S): MARPAT 136:401651
 GI



AB The title compds. I and their pharmaceutically acceptable salts, esters, prodrug esters, and stereoisomers are claimed (wherein: Z = CH(OH)CH2CR7(OH)CH2CO2R3 or corresponding pyranone lactone derivs.; n = 0, 1, x = 0, 1, 2, 3 or 4; provided that at least one of x and y is other than 0; and optionally one or more carbons of (CH2)x and/or (CH2)y together with addnl. carbons form a 3 to 7 membered spirocyclic ring; R1, R2 = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R3 = H or lower alkyl;

L4 ANSWER 4 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)
 IT 213252-19-8, KRP297
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (therapeutic compns. also contg.; prepn. of fused pyridine derivs. as HMG-CoA reductase inhibitors)
 RN 213252-19-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)

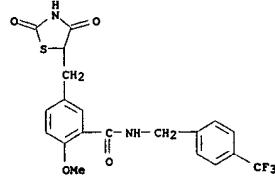


L4 ANSWER 5 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2002:142553 CAPLUS
 DOCUMENT NUMBER: 136:177969
 TITLE: Medicinal compositions containing PPAR.gamma.
 agonists
 and RXR agonists for preventing and treating
 cancer
 INVENTOR(S): Kurakata, Shinichi; Fujiwara, Kosaku;
 Shimazaki,
 PATENT ASSIGNEE(S): Naomi; Fujita, Takashi
 Sankyo Company, Limited, Japan
 SOURCE: PCT Int. Appl., 40 pp.
 CODEN: PIIXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002013864	A1	20020221	WO 2001-JP7037	20010815
W: AU, BR, CA, CN, CO, CZ, HU, ID, IL, IN, KR, MX, NO, NZ,				
PL, RU,				
SG, SK, US, ZA				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU,				
MC, NL,				
PT, SE, TR				
JP 2002128700	A2	20020509	JP 2001-241740	20010809
AU 2001078738	A5	20020225	AU 2001-78738	20010815
PRIORITY APPLN. INFO.:			JP 2000-246910 A	20000816
			JP 2000-2000246910A	20000816
			WO 2001-JP7037	W 20010815

OTHER SOURCE(S): MARPAT 136:177969
 AB Disclosed are medicinal compns. for preventing or treating cancer
 wherein
 one or more Peroxisome proliferator-activated receptor .gamma.
 (PPAR.gamma.) activation agonists and one or more retinoid X
 receptor
 (RXR) activation agonists are used simultaneously or successively.
 A combined administration of 5-[4-(6-methoxy-1-methylbenzimidazol-2-
 ylmethoxy)benzyl]thiazolidine-2,4-dione hydrochloride (I) 5 and
 targretin
 100 mg/kg to HL-60 cell-bearing mice showed synergistic antitumor
 effect.
 Also, tablets were prep'd. from I 0.004, targretin 0.1, lactose
 0.244, corn
 starch 50, and magnesium stearate 0.002 g.
 IT 213252-19-8
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (simultaneous or successive use of PPAR.gamma. agonists and RXR
 agonists for prevention or treatment of cancer)
 RN 213252-19-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinylmethyl)-2-methoxy-N-[(4-
 (trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 5 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L4 ANSWER 6 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2002:142506 CAPLUS
 DOCUMENT NUMBER: 136:177977
 TITLE: Methods for treating inflammatory diseases
 using PPAR
 agonists
 INVENTOR(S): Pershad Singh, Harrihar A.
 PATENT ASSIGNEE(S): USA
 SOURCE: PCT Int. Appl., 42 pp.
 CODEN: PIIXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

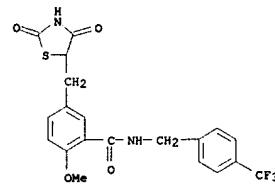
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002013812	A1	20020221	WO 2001-US25668	20010816
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RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU,				
MC, NL,				
PT, SE, TR				
AU 2001088271	A5	20020225	AU 2001-88271	20010816
PRIORITY APPLN. INFO.:			US 2000-225907P	20000817
			US 2000-230509P	20000906
			WO 2001-US25668	W 20010816

AB The present invention describes methods for the use of PPAR ligands in the treatment of inflammatory, endocrine, dermatol., cardiovascular immunol., neuro., ophthalmic, neoplastic, pulmonary diseases, and age-related dysregulations. In addn., methods are provided for treating said conditions and diseases comprising the step of administering to a human or an animal in need thereof a therapeutic amt. of pharmcol. compns. comprising a pharmaceutically acceptable carrier, and a PPAR.gamma. agonist which cross-activates PPAR.alpha. or PPAR.delta. or both, or a PPAR.gamma. partial agonist, or a PPAR.gamma./RXR agonist, effective to reverse, slow, stop, or prevent the pathol. inflammatory or degenerative process.

IT 213252-19-8, KRP 297
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (methods for treating inflammatory diseases using PPAR agonists)

RN 213252-19-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinylmethyl)-2-methoxy-N-[(4-
 (trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 6 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)

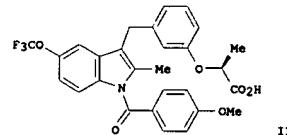
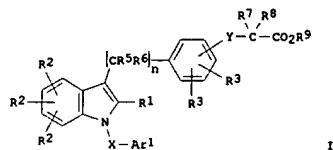


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L4 ANSWER 7 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2002:90008 CAPLUS
 DOCUMENT NUMBER: 136:151071
 TITLE: Preparation of N-substituted indoles for
 treating diabetes
 INVENTOR(S): Acton, John J., III; Black, Regina Marie;
 Jones, Anthony Brian; Wood, Harold Blair
 PATENT ASSIGNEE(S): Merck & Co., Inc., USA
 SOURCE: PCT Int. Appl., 73 pp.
 CODEN: PIIXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002008188	A1	20020131	WO 2001-US22979	20010720
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SI, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2002042441	A1	20020411	US 2001-912961	20010725
PRIORITY APPLN. INFO.:			US 2000-220778P	P 20000725
OTHER SOURCE(S):	MARPAT	136:151071		
GI				

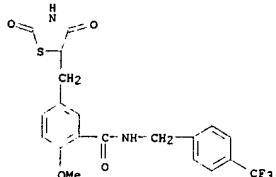
L4 ANSWER 7 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)



AB The title indoles having aryloxyacetic acid substituents (I; R1 = Me, optionally substituted with 1-3 F atoms; R2-R4 = H, halo, alkyl, etc.; R5, R6 = H, F, OH, alkyl; and R5 and R6 groups that are on the same carbon atom optionally may be joined to form a cyclopropyl group; R7, R8 = H, F, or CR7R8 may form cycloalkyl; R9 = H, alkyl; Ar1 = (un)substituted Ph, naphthyl, pyridyl, quinolyl; X = CO, SO2, CH2, CMe2, CF2, cyclopropylidene; Y = O, S; n = 0-5) which are agonists or partial agonists of PPAR gamma, and are useful in the treatment, control or prevention of non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR mediated diseases, disorders and conditions, were prep. E.g., a multi-step synthesis of (2S)-II was given.

IT 213252-19-8, KRP-297
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (prepn. of N-substituted indoles for treating diabetes)
 RN 213252-19-8 CAPLUS
 CN Benzanide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 7 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)

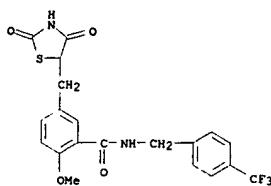


REFERENCE COUNT:
 FOR THIS
 RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L4 ANSWER 8 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2002:56491 CAPLUS
 DOCUMENT NUMBER: 137:73203
 TITLE: Pharmacological analysis of wild-type .alpha., .gamma., and .delta. subtypes of the human peroxisome proliferator-activated receptor
 AUTHOR(S): Murch, T.; Junquero, D.; Delhon, A.; Pauwels, P. J.
 CORPORATE SOURCE: Department of Cellular and Molecular Biology, Centre de Recherche Pierre Fabre, Castres, 81106, Fr.
 SOURCE: (2002), Naunyn-Schmiedeberg's Archives of Pharmacology 365 (2), 133-140
 PUBLISHER: Springer-Verlag
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Three distinct peroxisome proliferator-activated receptor (PPAR) cDNAs were isolated from human brain RNA. Whereas the PPAR.delta. subtype perfectly matched the amino acid sequences reported in the Genbank database, several differences were found for the PPAR.alpha. (Lys123Met, Ala268Val, Gly296Ala and Val444Ala) and PPAR.gamma.2 (Met81Le, Pro9Ala, Met186Ile, Pro187Ala and the deletion of a Gln213 residue) subtypes. A pharmacol. anal. was undertaken by co-expressing each PPAR subtype with a reporter plasmid contg. a luciferase gene under the transcriptional control of a synthetic, triplicated PPAR response element in either HepG2 or Cos-7 cells. Whereas fenofibrate unselectively activated the PPAR.alpha. and PPAR.delta. subtypes, the related BM-17.0744 compd. was more potent and selective for PPAR.alpha.. The thiazolidine dione derivs. rosiglitazone and pioglitazone were potent and selective PPAR.gamma.2 agonists. L-165041, reported as a selective and potent PPAR.delta. ligand, displayed in this specified transactivation system, apart from its highly efficacious PPAR.delta. agonist activity, partial and full agonism at, resp., PPAR.alpha. and PPAR.gamma.2 subtypes. In conclusion, transcriptional control of a luciferase gene by wild-type PPAR subtypes provides powerful recombinant assays to evaluate ligand's efficacy at these nuclear receptors.

IT 213252-19-8, KRP-297
 RL: PAC (Pharmacological activity); BIOL (Biological study)
 (pharmacol. anal. of wild-type .alpha., .gamma. and .delta. subtypes of

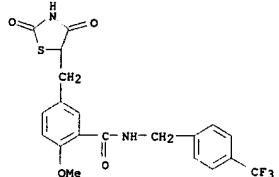
L4 ANSWER 8 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)
 human peroxisome proliferator-activated receptor
 RN 213252-19-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L4 ANSWER 9 OF 32 CAPLUS COPYRIGHT 2002 ACS
 2001:900080 CAPLUS
 ACCESSION NUMBER: 136:318816
 DOCUMENT NUMBER:
 TITLE: Design, synthesis and evaluation of substituted phenylpropanoic acid derivatives as peroxisome proliferator-activated receptor (PPAR) activators:
 novel human PPAR. α -selective activators
 AUTHOR(S): Miyachi, Hiroyuki; Nomura, Masahiro; Tanase,
 Takahiro;
 Masaki;
 CORPORATE SOURCE: Murakami, Koji; Awano, Katsuya
 Research Kyorin Pharmaceutical Co., Ltd., Discovery
 Laboratories, Tochigi, Shimotsuga-gun,
 Nogi-machi, 329-0114, Japan
 SOURCE: Bioorganic & Medicinal Chemistry Letters
 (2001), → Volume Date 2002, 12(1), 77-80
 PUBLISHER: CODEN: BMCLE8; ISSN: 0960-894X
 Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB A series of substituted phenylpropanoic acid derivs. was prep'd. as part of a search for subtype-selective human peroxisome proliferator-activated receptor (PPAR) activators. Structure-activity relationship studies indicated that the substituent at the . α -position of the carboxyl group plays a key role in detg. the potency and the selectivity for PPAR transactivation.
 IT 213252-19-8, KRP 297
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (design, synthesis and evaluation of substituted phenylpropanoic acid derivs. as PPAR activators)
 RN 213252-19-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)

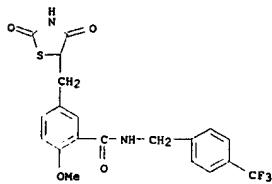
L4 ANSWER 9 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L4 ANSWER 10 OF 32 CAPLUS COPYRIGHT 2002 ACS
 2001:798208 CAPLUS
 ACCESSION NUMBER: 135:344474
 DOCUMENT NUMBER:
 TITLE: Preparation of novel stable crystal of thiazolidinedione derivative
 INVENTOR(S): Onoda, Michiyo; Orita, Kazuo
 PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 17 pp.
 PUBLISHER: CODEN: PIXXDZ
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

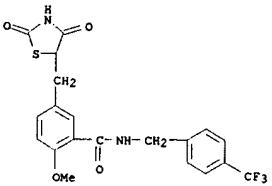
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001081327	A1	20011101	WO 2001-JP3450	20010423
CH, CN,	W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MR, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG		JP 2000-124006	A 20000425
AB	Priority APPLN. INFO.: Claimed is a crystal of 5-[(2,4-dioxothiazolidin-5-yl)methyl]-2-methoxy-N- [(4-(trifluoromethyl)phenyl)methyl]benzamide (KRP-297) having diffraction angles (2. θ) at at least 9.7.degree., 15.0.degree., and 22.5.degree. in X-ray powder diffractometry. The novel crystal of KRP-297 (a known antidiabetic agent) is prep'd. through recrystn. from an alc. solvent.			
IT 353275-24-8P	RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent) (prepn. of novel stable crystal of thiazolidinedione deriv.)			
RN 353275-24-8 CAPLUS	CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]-, monosodium salt (9CI) (CA INDEX NAME)			



● Na

IT 213252-19-8P, KRP-297

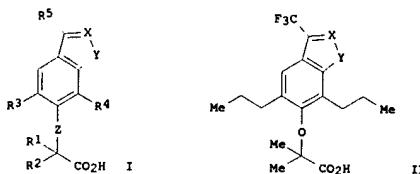
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation);
 USES
 (Uses)
 (prepn. of novel stable crystal of thiazolidinedione deriv.)
 RN 213252-19-8 CAPLUS
 CN Benzamide, 5-[{2,4-dioxo-5-thiazolidinyl}methyl]-2-methoxy-N-[{4-(trifluoromethyl)phenyl}methyl]- (9CI) (CA INDEX NAME)



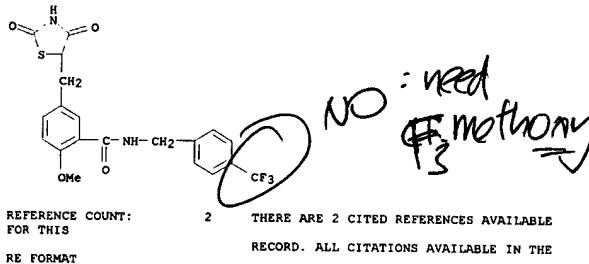
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L4 ANSWER 11 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:617987 CAPLUS
 DOCUMENT NUMBER: 135:180757
 TITLE: Preparation of 1,2-benzoxazolylloxyacetic acids
 and
 diabetes and analogs as PPAR agonists for treatment of
 lipid disorders
 INVENTOR(S): Liu, Kun; Xu, Libo; Jones, A. Brian
 PATENT ASSIGNEE(S): Merck & Co. Inc., USA
 SOURCE: PCT Int. Appl., 54 pp.
 CODEN: PIIXKD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060807	A1	20010823	WO 2001-US4636	20010214
CH, CN, CN, HR, LT, LU, RU, SD, VN, YU,	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LV, MA, MD, MG, MK, MN, MW, MZ, NO, NZ, PL, PT, RO, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, ZA, ZM, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
CH, CY, TR, BF,	DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
PRIORITY APPLN. INFO.: US 2000-183593P	OTHER SOURCE(S): MARPAT 135:180757	GI	GI	20000218



AB The title compds. (I) [wherein R1 and R2 = independently H, F, (halo)alkyl, (halo)alkenyl, (halo)alkynyl; or R1 and R2 may form a cycloalkyl group; R3 and R4 = independently (fluoro)alkyl, (fluorocycloalkyl, (fluoro)alkynyl, or Cl; X = N or CR; Y = O, S, nor NR; Z = O or S; R = independently H or optionally fluoro- or alkoxy-substituted (cycle)alkyl(oxy), alkenyl(oxy), or alkynyl(oxy); R5 = H or (un)substituted alkyl, alkenyl, alkynyl, (hetero)aryl(oxy), heterocycl(oxy), etc.; and pharmaceutically acceptable salts and prodrugs thereof] were prep'd. For example, 2,4-dihydroxy-3,5-dipropyl-1',1',1'-trifluoracetophenone oxime was acetylated and then treated with pyridine and TEA to give 5,7-dipropyl-6-hydroxy-3-trifluoromethyl-1,2-benzisoxazole. Etherification with Me .alpha.-bromoiso butyrate in the presence of Cs2CO3 in DMF, followed by sapon., afforded the 1,2-benzoxazolylloxyacetic acid (II). I are potent agonists of peroxisome proliferator activated receptor (PPAR) .alpha. and/or .gamma. and are useful in the treatment, control, or prevention of non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR.alpha. and/or .gamma. mediated diseases, disorders, and conditions (no data).
 IT 213252-19-8, KRP-297
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
 (Uses)
 (coadministration with; prepn. of benzisoxazolylloxyacetic acid
 PPAR agonists via cyclization of dihydroxyacetophenone oximes for treatment of diabetes and lipid disorders)
 → RN 213252-19-8 CAPLUS
 CN Benzamide, 5-[{2,4-dioxo-5-thiazolidinyl}methyl]-2-methoxy-N-[{4-(trifluoromethyl)phenyl}methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE
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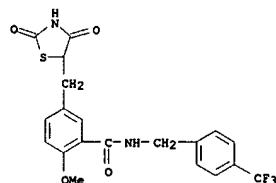
L4 ANSWER 12 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:617810 CAPLUS
 DOCUMENT NUMBER: 135:175429
 TITLE: Modulation of bone formation with peroxisome proliferator-activated receptor activators and ligands

INVENTOR(S): Scutt, Andrew; Still, Karen
 PATENT ASSIGNEE(S): University of Sheffield, UK
 SOURCE: PCT Int. Appl., 27 pp.
 CODEN: PIXXD2

DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001060355	A1	20010823	WO 2001-GB626	20010215
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.: AB			GB 2000-3310	A 20000215
The use of an activator or ligand of a peroxisome proliferator-activated receptor, other than PPAR γ , or pharmaceutically acceptable deriv. of said activator or ligand, in the manuf. of a medicament for the treatment or prophylaxis of bone disease allows, for the first time, bone anabolism to enhance the deposition of bone in conditions which would benefit from increased bone deposition. The reverse, where there is inhibition and/or retardation of bone deposition is also facilitated.				
IT 213252-19-8, KRP-297				
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)				
(modulation of bone formation with peroxisome proliferator-activated receptor activators and ligands)				

L4 ANSWER 12 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)
 RN 213252-19-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 32 CAPLUS COPYRIGHT 2002 ACS

ACCESSION NUMBER: 2001:581862 CAPLUS
 DOCUMENT NUMBER: 135:152800

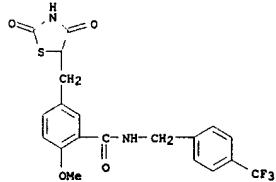
TITLE: Alkali metal salt of thiazolidine-2,4-dione derivative

INVENTOR(S): Ohnoda, Michiro; Orita, Kazuo; Yoshida, Noriyuki
 PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 17 pp.
 CODEN: PIXXD2

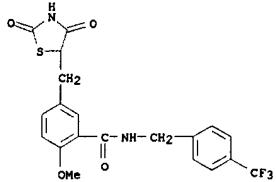
DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001057007	A1	20010809	WO 2001-JP598	20010130
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.: AB			JP 2000-23610	A 20000201
This document discloses a method of industrially advantageously purifying 5-[(2,4-dioxothiazolidin-5-yl)methyl]-2-methoxy-N-(4-(trifluoromethyl)phenyl)methylbenzamide (KRP-297), a known antidiabetic agent. The method comprises the steps of: forming an alkali metal salt of KRP-297 and a hydrate thereof in a reaction for producing KRP-297; isolating and purifying them; and then liberating the KRP-297 from the salt. Also provided are an alkali metal salt of KRP-297 and a hydrate of the salt.				
IT 213252-19-8P, KRP 297				
RL: PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)				
(purifn. of antidiabetic KRP-297)				
RN 213252-19-8 CAPLUS				

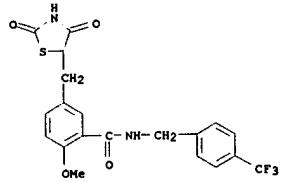
L4 ANSWER 13 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



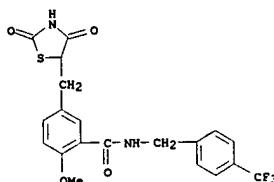
IT 353275-24-8P 353275-26-0P 353275-27-1P
 353275-28-2P
 RL: SPN (Synthetic preparation); PREP (Preparation)
 (purifn. of antidiabetic KRP-297)
 RN 353275-24-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]-, monosodium salt (9CI) (CA INDEX NAME)



● Na
 RN 353275-26-0 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]-, monosodium salt, monohydrate (9CI) (CA INDEX NAME)



● Na

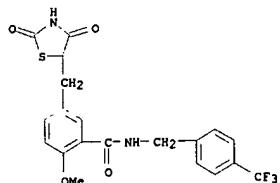


● K

● H₂O

RN 353275-27-1 CAPLUS
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]-, monopotassium salt (9CI) (CA INDEX NAME)

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT



● K

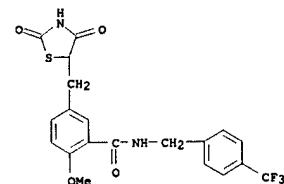
RN 353275-28-2 CAPLUS
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]-, monopotassium salt, monohydrate (9CI) (CA INDEX NAME)

L4 ANSWER 14 OF 32 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:564869 CAPLUS
DOCUMENT NUMBER: 135:132451
TITLE: Novel remedies with the use of .beta.3 agonists
INVENTOR(S): Ogawa, Kohhei; Umeno, Hiroshi
PATENT ASSIGNEE(S): Asahi Kasei K. K., Japan
SOURCE: PCT Int. Appl., 49 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001054728	A1	20010802	WO 2001-JP553	20010126
W:	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, GM, HR, LS, LT, RO, RU, UZ, VN, RW:	CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM GH, KE, IS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,	AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, GM, HR, LS, LT, RO, RU, UZ, VN, RW:	2000-20733 A 20000128

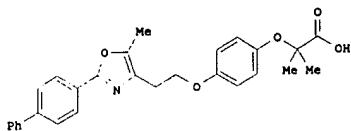
PRIORITY APPLN. INFO.: JP 2000-20733 A 20000128
AB Remedies contg. at least one member selected from the group consisting of cholinolytics, monoamine reuptake inhibitors, lipase inhibitors, selective serotonin reuptake inhibitors, insulin, insulin secretion promoters, biguanide, .alpha.-glucosidase inhibitors, insulin resistance improving agents, HMC-CoA reductase inhibitors, anion exchange resins, clofibrate-base drugs and nicotinic acid-base drugs and a compd. having a .beta.3-agonistic activity. The .beta.3 agonist has an activity of inhibiting urination disorder. When used together with a remedy for urination disorder such as propiverine, oxybutynin hydrochloride or tolterodine, it exerts an enhanced anti-urination disorder effect. When used together with an antibesity agent such as sibutramine or orlistat, it exerts an enhanced antibesity effect. When used together with an antidiabetic agent such as insulin, glibenclamide, acarbose or rosiglitazone, it exerts an enhanced antidiabetic effect. When used

L4 ANSWER 14 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)
together with an antilipemic drug such as bezafibrate or pravastatin, it exerts an enhanced antilipemic effect.
IT 213252-19-8, KRP 297
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel remedies with the use of .beta.3 agonists as antidiabetics and antilipidemics and for treatment of urination disorder)
RN 213252-19-8 CAPLUS
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

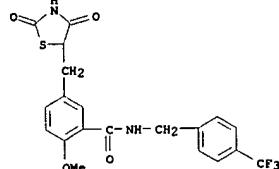
L4 ANSWER 15 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:367156 CAPLUS
 DOCUMENT NUMBER: 135:131731
 TITLE: Design and Synthesis of
 2-Methyl-2-[4-(2-(5-methyl-2-
 aryloxazol-4-yl)ethoxy]phenoxy]propionic
 Acids: A New
 Class of Dual PPAR. α ./. γ . Agonists
 AUTHOR(S): Brooks, Dawn A.; Etgen, Garret J.; Rito,
 J.; Shuker, Anthony J.; Dominianni, Samuel J.;
 Warshawsky, Alan M.; Ardecky, Robert;
 Paterniti, James R.; Tyhonas, John; Karanewsky, Donald S.;
 Kauffman, Raymond F.; Broderick, Carol L.; Oldham, Brian
 A.; Montrose-Rafizadeh, Chahzrad; Wineroski,
 Leonard L.; Paul, Margaret M.; McCarthy, James R.
 CORPORATE SOURCE: Lilly Research Laboratories A Division of Eli
 Company Lilly Corporate Center, Indianapolis,
 IN, 46285, USA
 SOURCE: Journal of Medicinal Chemistry (2001), 44(13),
 2061-2064
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB Propionic acid deriv. I, which was designed and synthesized based on putative pharmacophores of known PPAR. γ - and PPAR. α -selective compds., exhibits potent dual PPAR. α ./. γ . agonist activity as demonstrated by in vitro binding and dose overlap in the newly introduced EOB mouse model for glucose lowering and lipid/cholesterol homeostasis.

IT 213252-19-8, KRP-297

L4 ANSWER 15 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)
 RL: BAC (Biological activity or effector, except adverse); BSU
 (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (design and synthesis of
 2-methyl-2-[4-(2-(5-methyl-2-aryloxazol-4-yl)ethoxy]phenoxy]propionic acids: a new class of dual PPAR. α ./. γ . agonists)
 RN 213252-19-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)

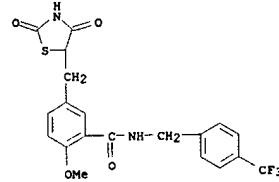


REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L4 ANSWER 16 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:359797 CAPLUS
 DOCUMENT NUMBER: 134:344620
 TITLE: Solid oral composition containing KRP-297
 INVENTOR(S): Ohyama, Toshinori; Imamura, Masaru
 PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 11 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001034148	A1	20010517	WO 2000-JP7905	20001110
W:	AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, ID, IL, LV, MD, SI, SK, AZ, BY,			
	CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, KG, KZ, MD, RU, TJ, TM RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG			
PRIORITY APPLN. INFO.:				JP 1999-320586 A 19991111
AB	Disclosed are solid compns. for oral use for facilitating the administration in a small dose of KRP-297, which is a ligand common to peroxisome proliferator-activated receptors PPAR. α . and PPAR. γ . (i.e., nuclear receptors) and has an effect of ameliorating insulin resistance, which contain the drug ingredient in a uniform content and can be easily and quant. taken. By prepg. solid compns. for oral use composed of a trace amt. of the drug ingredient together with pharmaceutical carriers, it is possible to provide tablets which contain the drug component in a uniform content and can be easily and quant. taken.			
A	film-coated tablet was prep. from KRP-297 0.25, lactose 78.55, cryst. cellulose 26.2, low-substituted hydroxypropyl cellulose 12, polyvinyl alc. 2.4, magnesium stearate 0.6, hydroxypropyl Me cellulose, and carnauba wax 0.001 mg.			
IT 213252-19-8, KRP-297	RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (solid oral compns. contg. uniform contents of KRP-297)			

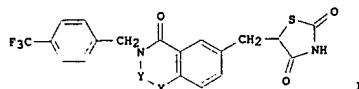
L4 ANSWER 16 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)
 RN 213252-19-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE
 FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L4 ANSWER 17 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:347100 CAPLUS
 DOCUMENT NUMBER: 134:353303
 TITLE: preparation of thiazolidinyl-containing
 bicyclic heterocycles as humane peroxisome proliferator-activated receptor .gamma. agonists
 INVENTOR(S): Nomura, Masahiro; Murakami, Koji; Kakuta, Masaki
 PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
 CODEN: JKOKAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 2001131173	A2	20010515	JP 2000-242708	20000810
PRIORITY APPLN. INFO.:			JP 1999-235531	A 19990823
OTHER SOURCE(S):	MARPAT 134:353303			
GI				

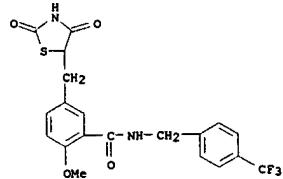


AB Title compds. I (YX = CO₂, CH₂O, CH:CH), their pharmaceutically acceptable salts, or hydrates, useful as for treatment of Type II diabetes and hyperlipidemia, are prep'd. 2-Hydroxy-5-[(2,4-dioxothiazolidin-5-yl)methyl]-N-[(4-trifluorophenyl)methyl]benzamide was reacted with trioxane in the presence of AcOH in CH₂Cl₂ at room temp. for 2 day to give 42% 6-[(2,4-dioxothiazolidin-5-yl)methyl]-3-[(4-trifluorophenyl)methyl]-1,3-benzoxazin-4-one showing good transcription activity of proliferator-activated receptor .gamma. in vitro.

IT 213252-19-8
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (prepn. of bicyclic heterocycles as humane peroxisome proliferator-activated receptor .gamma. agonists)

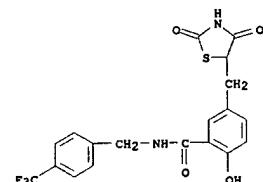
RN 213252-19-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 17 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)



IT 223508-81-4P
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (prepn. of bicyclic heterocycles as humane peroxisome proliferator-activated receptor .gamma. agonists)

RN 223508-81-4 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-hydroxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 18 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:338335 CAPLUS
 DOCUMENT NUMBER: 134:344604
 TITLE: Antidiabetic formulation containing metformin and sulfonylurea
 INVENTOR(S): Piper, Beth Anne
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
 SOURCE: PCT Int. Appl., 76 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

5 (0.00)

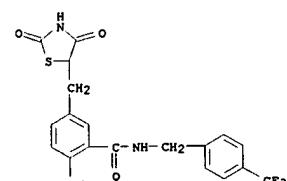
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001032158	A2	20010510	WO 2000-US28467	20001013
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IB, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
PRIORITY APPLN. INFO.:			US 1999-432465	A 19991103
AB A low dose antidiabetic formulation adapted for treating e.g., Type II diabetes contains a combination of metformin (at <800 mg/day) and at least 1 other antidiabetic agent such as a sulfonylurea. This combination provides at least about substantially equiv. efficacy in treating diabetes as do antidiabetic formulations contg. metformin employed in dosages prescribed in generally accepted medical practice for first line therapy in treating diabetes, but with substantially reduced side effects, such as hypoglycemia and/or gastrointestinal distress. A method for treating diabetes in drug naive human patients is also provided employing the above formulation to reduce insulin resistance and/or post-prandial glucose excursion and/or Hb 1AC, and/or increase post-prandial insulin, thereby				

L4 ANSWER 18 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)
 treating the diabetes. Thus, tablets contained metformin-HCl 250.0,
 glyburide 1.25, croscarmellose sodium 7.00, Povidone 10.00,
 microcryst.

cellulose 28.25, Mg stearate 2.25, and HPMC film-coating 6 mg. The effectiveness of this combination drug in producing hypoglycemia was demonstrated clin.

IT 213252-19-8, KRP-297
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antidiabetic formulation contg. metformin and sulfonylurea)
 RN 213252-19-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 19 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:283949 CAPLUS
 DOCUMENT NUMBER: 134:311218
 TITLE: Synthesis and use of heterocyclic sodium/proton exchange inhibitors
 INVENTOR(S): Ahmad, Saleem; Wu, Shung C.; O'Neil, Steven
 V.: Ngu, Kheyong; Atwal, Karmail S.
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
 SOURCE: PCT Int. Appl., 221 pp.
 CODEN: PIIXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

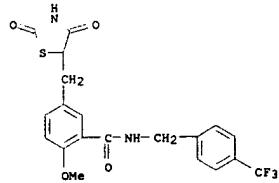
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001027107	A2	20010419	WO 2000-US27461	20001002
WO 2001027107	A3	20020124		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, T2, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG EP 1224183 A2 20020724 EP 2000-968723 20001002 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL NO 2002001717 A 20020610 NO 2002-1717 20020411 PRIORITY APPLN. INFO.: US 1999-158755P P 19991012 WO 2000-US27461 W 20001002				

OTHER SOURCE(S): MARPAT 134:311218
GI

L4 ANSWER 19 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)

AB Compds. of formula I [wherein; n is 1-5; X is N or CR5, where R5 is H, halo, alkenyl, alkynyl, alkoxy, alkyl, aryl or heteroaryl; Z is a heteroaryl group; R1 is H, alk(en)(ynyl), alk(enyl)(ynyl)oxy, (aryl or alkyl)3Si, cycloalk(en)yl, (aryl)amino, aryl(alkyl), cycloalkenyl, etc.]; R2, R3 and R4 are any of the groups set out for R1 and optionally substituted with 1 to 5 substituents which may be the same or different and when X is N, R1 is preferably aryl or heteroaryl] are claimed. Several hundred examples are disclosed. Synthesis of II proceeds via cyclopropanation of the cinnamate derived from the olefination between 3,5-dichlorobenzaldehyde and t-butylidethylphosphonoacetate. The intermediate tert-Bu ester is converted to the corresponding alpha,-chloroketone and reacted with acetyl guanidine to provide II in a total of 5 steps. Compds. I are said to be sodium/proton exchange inhibitors (NHE). Pharmaceutical combinations are claimed using I and certain antihypertensive agents, .beta.-adrenergic agonists, hypolipidemic agents, antidiabetic agents, antiobesity agents, etc. Compds. I are useful as antianginal and cardioprotective agents and provide a method for preventing or treating angina pectoris, cardiac dysfunction, myocardial necrosis, and arrhythmia. IT 213252-19-8, KR297 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (pharmaceuticals also contg.; synthesis and use of heterocyclic sodium/proton exchange inhibitors) RN 213252-19-8 CAPLUS CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl] (9CI) (CA INDEX NAME)

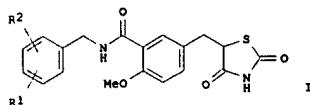
L4 ANSWER 19 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)



L4 ANSWER 20 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2001:152661 CAPLUS
 DOCUMENT NUMBER: 134:193428
 TITLE: Preparation of substituted benzylthiazolidine-2,4-dione derivatives as agonists of human peroxisome proliferator-activated receptor
 INVENTOR(S): Nomura, Masahiro; Murakami, Koji; Tsunoda, Masaki; Takahashi, Yukie
 PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 19 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

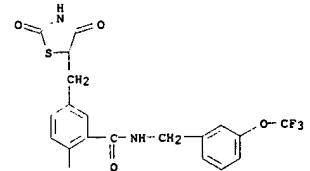
PRIORITY APPLN. INFO.: JP 1999-235530 A 19990823
 NO 2000-JP5522 W 20000818
 OTHER SOURCE(S): MARPAT 134:193428
GI

371 of
✓ PCT

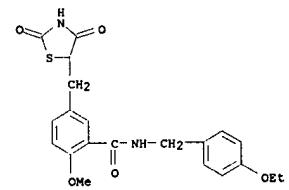


AB The title compds. (I), pharmaceutically acceptable salts thereof and hydrates of the same (wherein R₁ represents chloro, bromo, nitro, trifluoromethoxy, ethoxy, propoxy or isopropoxy; and R₂ represents hydrogen or chloro) are prep'd. These compds. are capable of, as a ligand of human peroxisome proliferator-activated receptor (PPAR), enhancing the transcriptional activity of the receptor and showing effects of lowering blood sugar level and lowering lipid level; and a process for producing the same. Thus, 5-((2,4-dioxothiazolidin-5-yl)methyl)-2-methoxybenzoic acid, Et₃N, and CH₂Cl₂ were mixed, treated with Et₃COCO₂Et and stirred under ice-cooling for 10 min, treated with 4-nitrobenzylamine, and then stirred at room temp. for 2 h to give 75% N-((4-nitrophenyl)methyl)-5-((2,4-dioxothiazolidin-5-yl)methyl)-2-methoxybenzamide (II). II and I (R₁ = 4-n-Pr, R₂ = H) enhanced the transcriptional activity of human PPAR alpha, in CHO cells with EC₅₀ of 0.53 and 0.11 μM, resp. ITN 326926-46-0P 326926-47-0P 326926-48-1P 326926-49-2P 326926-50-5P 326926-51-6P 326926-52-7P 326926-53-8P 326926-54-9P, RN 326926-46-0P 326926-47-0P 326926-48-1P 326926-49-2P 326926-50-5P 326926-51-6P 326926-52-7P 326926-53-8P 326926-54-9P, CN Benzamide, 5-((2,4-dioxothiazolidin-5-yl)methyl)-2-methoxy-N-((4-nitrophenyl)methyl)- (9CI) (CA INDEX NAME)

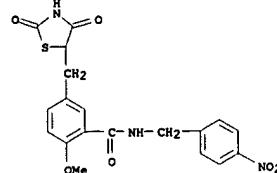
L4 ANSWER 20 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)
RN 326926-49-2 CAPLUS
CN Benzamide, 5-((2,4-dioxothiazolidin-5-yl)methyl)-2-methoxy-N-((3-trifluoromethoxyphenyl)methyl)- (9CI) (CA INDEX NAME)



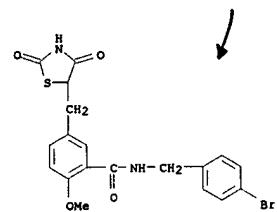
RN 326926-50-5 CAPLUS
CN Benzamide, 5-((2,4-dioxothiazolidin-5-yl)methyl)-N-((4-ethoxyphenyl)methyl)-2-methoxy- (9CI) (CA INDEX NAME)



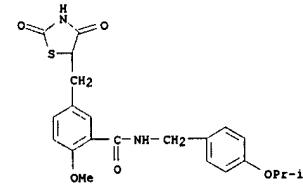
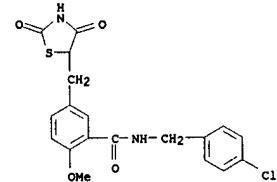
RN 326926-51-6 CAPLUS
CN Benzamide, 5-((2,4-dioxothiazolidin-5-yl)methyl)-2-methoxy-N-((4-(1-methylethoxy)phenyl)methyl)- (9CI) (CA INDEX NAME)



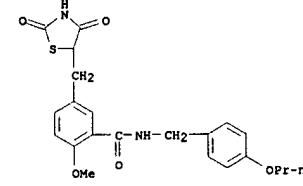
RN 326926-47-0 CAPLUS
CN Benzamide, N-((4-bromophenyl)methyl)-5-((2,4-dioxothiazolidin-5-yl)methyl)-2-methoxy- (9CI) (CA INDEX NAME)



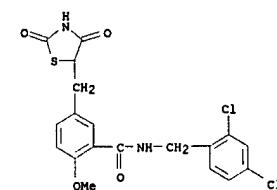
RN 326926-48-1 CAPLUS
CN Benzamide, N-((4-chlorophenyl)methyl)-5-((2,4-dioxothiazolidin-5-yl)methyl)-2-methoxy- (9CI) (CA INDEX NAME)



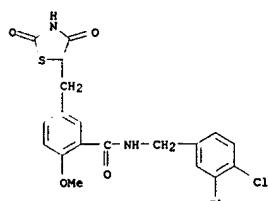
RN 326926-52-7 CAPLUS
CN Benzamide, 5-((2,4-dioxothiazolidin-5-yl)methyl)-2-methoxy-N-((4-propoxymethyl)methyl)- (9CI) (CA INDEX NAME)



RN 326926-53-8 CAPLUS
CN Benzamide, N-((2,4-dichlorophenyl)methyl)-5-((2,4-dioxothiazolidin-5-yl)methyl)-2-methoxy- (9CI) (CA INDEX NAME)



L4 ANSWER 20 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)
RN 326926-54-9 CAPLUS
CN Benzamide, N-[(3,4-dichlorophenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)

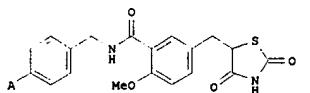


REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L4 ANSWER 21 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)
ACCESSION NUMBER: 2001:152660 CAPLUS
DOCUMENT NUMBER: 134:193427
TITLE: Preparation of substituted benzylthiazolidine-2,4-dione derivatives as agonists of human peroxisome proliferator-activated receptor
INVENTOR(S): Miyachi, Hiroyuki; Nomura, Masahiro; Tanase, Takahiro;
PATENT ASSIGNEE(S): Murakami, Koji; Tsunoda, Masaki Kyorin Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

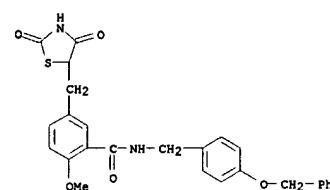
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014351	A1	20010301	WO 2000-0P5521	20000818
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1207157	A1	20020522	EP 2000-953477	20000818
PRIORITY APPLN. INFO.: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL			JP 1999-235529 A 19990823	
			JP 2000-242707 A 20000810	
			WO 2000-JP5521 W 20000818	
OTHER SOURCE(S): MARPAT 134:193427				
GI				

L4 ANSWER 21 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)

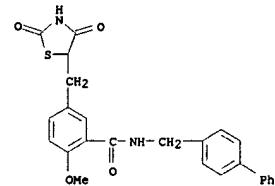


AB The title compds. represented by general formula (I; wherein A represents optionally substituted Ph, optionally substituted phenoxy or optionally substituted benzyloxy), pharmaceutically acceptable salts thereof and hydrates of the same are prep'd. These compds. are capable of, as a ligand of human peroxisome proliferator-activated receptor (PPAR), enhancing the transcriptional activity of the receptor and showing effects of lowering blood sugar level and lowering lipid level. Thus, 5-[(2,4-dioxothiazolidin-5-ylmethyl)-2-methoxybenzoic acid, Et3N, and CH2Cl2 were mixed, treated with Et chlorocarbonate under ice-cooling, and stirred for 10 min under ice-cooling, followed by adding a soln. of 4-benzyloxybenzylamine in CH2Cl2, and the resulting mixt. was stirred at room temp. for 2 h to give 77% N-[(4-benzyloxyphenyl)methyl]-5-[(2,4-dioxothiazolidin-5-yl)methyl]-2-methoxybenzamide (II). II and I (A = PhO) enhanced the transcriptional activity of human PPAR. α . in CHO cells with EC50 of 0.44 and 0.24 .mu.M, resp.
IT 326925-77-3 326925-78-4P 326925-79-5P
326925-80-8P 326925-81-9P 326925-82-0P
326925-83-1P 326925-84-2P 326925-85-3P
326925-86-4P 326925-87-5P 326925-88-6P
326925-89-7P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prepn. of substituted benzylthiazolidinedione derivs. as agonists of human peroxisome proliferator-activated receptor and blood sugar and lipid-lowering agents)
RN 326925-77-3 CAPLUS
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-phenylmethoxy)phenyl]methyl- (9CI) (CA INDEX NAME)

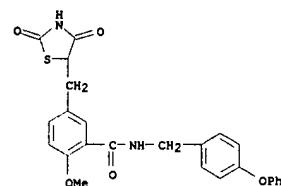
L4 ANSWER 21 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 326925-78-4 CAPLUS
CN Benzamide, N-[(1,1'-biphenyl)-4-ylmethyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)

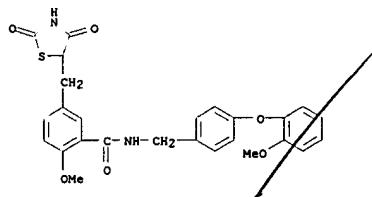


RN 326925-79-5 CAPLUS
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-phenoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

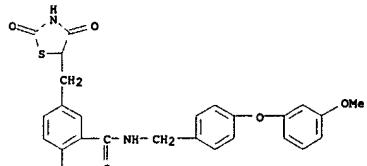


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of PCT
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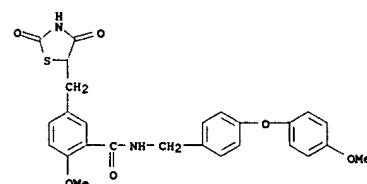
RN 326925-80-8 CAPLUS
 CN Benzamide,
 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(2-methoxyphenoxy)phenyl)methyl]- (9CI) (CA INDEX NAME)



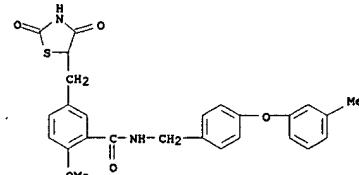
RN 326925-81-9 CAPLUS
 CN Benzamide,
 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(3-methoxyphenoxy)phenyl)methyl]- (9CI) (CA INDEX NAME)



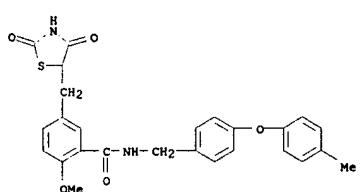
RN 326925-82-0 CAPLUS
 CN Benzamide,
 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(4-methoxyphenoxy)phenyl)methyl]- (9CI) (CA INDEX NAME)



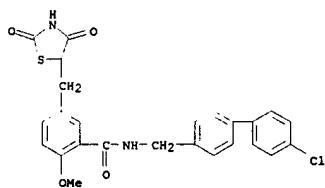
RN 326925-83-1 CAPLUS
 CN Benzamide,
 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(3-methoxyphenoxy)phenyl)methyl]- (9CI) (CA INDEX NAME)



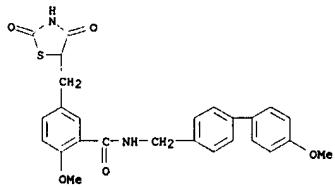
RN 326925-84-2 CAPLUS
 CN Benzamide,
 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(4-methoxyphenoxy)phenyl)methyl]- (9CI) (CA INDEX NAME)



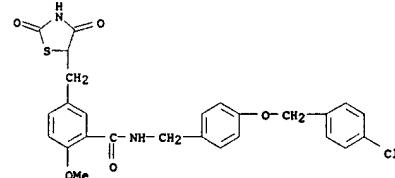
RN 326925-85-3 CAPLUS
 CN Benzamide,
 N-[(4'-chloro[1,1'-biphenyl]-4-yl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)



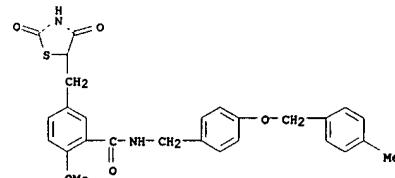
RN 326925-86-4 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4'-methoxy[1,1'-biphenyl]-4-yl)methyl]- (9CI) (CA INDEX NAME)



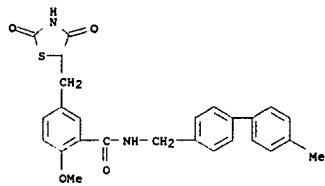
RN 326925-87-5 CAPLUS
 CN Benzamide,
 N-[(4-[(4-chlorophenyl)methoxy]phenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)



RN 326925-88-6 CAPLUS
 CN Benzamide,
 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(4-methoxyphenyl)methoxy)phenyl)methyl]- (9CI) (CA INDEX NAME)



RN 326925-89-7 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-methyl[1,1'-biphenyl]-4-yl)methyl]- (9CI) (CA INDEX NAME)

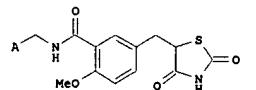


REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

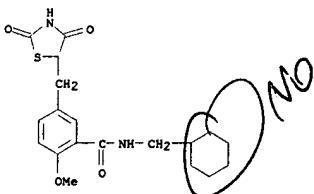
L4 ANSWER 22 OF 32 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 2001:152659 CAPLUS
DOCUMENT NUMBER: 134:178551
TITLE: Preparation of substituted benzylthiazolidine-2,4-dione derivatives as ligands of human peroxisome
INVENTOR(S): Masaki Fujimori, Shizuyoshi; Murakami, Koji; Tsunoda,
PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 18 pp.
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001014350	A1	20010301	WO 2000-JP5520	20000818
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, A2, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1207156	A1	20020522	EP 2000-953476	20000818
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
PRIORITY APPLN. INFO.: JP 1999-235528 A 19990823				
			WO 2000-JP5520	W 20000818
			GI	

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S71.



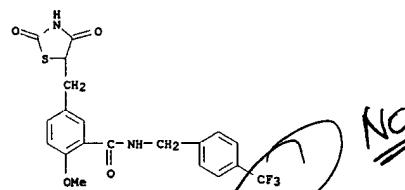
L4 ANSWER 22 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)
AB The title compds. (I; wherein A represents pyridyl or cyclohexyl), pharmaceutically acceptable salts thereof and hydrates of the same are prepd. These compds. are capable of, as a ligand of human peroxisome proliferator-activated receptor (PPAR), enhancing the transcriptional activity of the receptor and showing effects of lowering blood sugar level and lowering lipid level. Thus, 5-[(2,4-dioxothiazolin-5-yl)methyl]-2-methoxybenzoic acid, 2-picolyamine, 1-ethyl-3-(3-dimethylaminopropyl)carbodiimide hydrochloride, and DMF were stirred at room temp. overnight to give 20% I (A = 2-pyridyl) (II). II and I (A = 4-pyridyl) enhanced the transcriptional activity of human PPAR.alpha. in CHO cells with EC50 of 0.353 and 0.235 .mu.M, resp., and that of human PPAR.gamma. with EC50 of 0.30 and 0.14 .mu.M, resp.
IT 326922-18-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prep. of substituted benzylthiazolidinedione derivs. as ligands of human peroxisome proliferator-activated receptor and blood sugar and lipid-lowering agents)
RN 326922-18-3 CAPLUS
CN Benzanide,
N-(cyclohexylmethyl)-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:293302 CAPLUS
 DOCUMENT NUMBER: 133:84110
 TITLE: Fenofibrate and Rosiglitazone Lower Serum Triglycerides with Opposing Effects on Body Weight
 AUTHOR(S): Chaput, Evelyne; Saladin, Regis; Silvestre, Martine;
 CORPORATE SOURCE: Edgar, Alan D.
 Department of Metabolic Diseases, Laboratoire Fournier, Daix, 21121, Fr.
 SOURCE: Biochemical and Biophysical Research Communications
 (2000), 271(2), 445-450
 PUBLISHER: CODEN: BBRCAR; ISSN: 0006-291X
 DOCUMENT TYPE: Academic Press
 JOURNAL
 LANGUAGE: English
 AB Activators of peroxisome proliferator activated receptors (PPARs) are effective drugs to improve the metabolic abnormalities linking hypertriglyceridemia to diabetes, hyperglycemia, insulin-resistance, and atherosclerosis. We compared the pharmacol. profile of a PPAR.alpha. activator, fenofibrate, and a PPAR.gamma. activator, rosiglitazone, on serum parameters, target gene expression, and body wt. gain in (fa/fa) fatty Zucker rats and db/db mice as well as their assocn. in db/db mice. Fenofibrate faithfully modified the expression of PPAR.alpha. responsive genes. Rosiglitazone increased adipose tissue aP2 mRNA in both models while increasing liver acyl CoA oxidase mRNA in db/db mice but not in fatty Zucker rats. Both drugs lowered serum triglycerides yet rosiglitazone markedly increased body wt. gain while fenofibrate decreased body wt. gain in fatty Zucker rats. KRP 297, which has been reported to be a PPAR.alpha. and .gamma. co-activator, also affected serum triglycerides and insulin in fatty Zucker rats although no change in body wt. gain was noted. These results serve to clearly differentiate the metabolic finality of two distinct classes of drugs, as well as their corresponding nuclear receptors, having similar effects on serum triglycerides. (c) 2000 Academic Press.
 IT 213252-19-8, KRP 297
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study) (fenofibrate and rosiglitazone lower serum triglycerides with opposing

L4 ANSWER 23 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)
 effects on body wt.)
 RN 213252-19-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

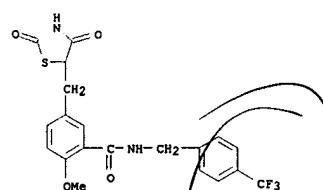


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 21 THERE ARE 21 CITED REFERENCES AVAILABLE
 RECORD. ALL CITATIONS AVAILABLE IN THE

L4 ANSWER 24 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:243901 CAPLUS
 DOCUMENT NUMBER: 133:12622
 TITLE: Tissue-specific actions of antidiabetic thiazolidinediones on the reduced fatty acid oxidation
 diabetic fatty in skeletal muscle and liver of zucker
 AUTHOR(S): Ide, Tomohiro; Nakazawa, Tomoko; Mochizuki, Toshiro;
 CORPORATE SOURCE: Murakami, Koji
 Central Research Laboratories, Kyorin Pharmaceutical,
 Tochigi, 329-0114, Japan
 SOURCE: Metabolism, Clinical and Experimental (2000), 49(4), 521-525
 PUBLISHER: CODEN: METAAJ; ISSN: 0026-0495
 W. B. Saunders Co.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Fatty acid overload has been proposed as a cause of decreased responsiveness in the major insulin target tissues of the body such as muscle and liver tissue. We therefore investigated fatty acid oxidn. in soleus muscle and liver isolated from Zucker diabetic fatty (ZDF) rats treated with thiazolidinediones, a new class of antidiabetic agents. ¹⁴C02 prodn. from [¹⁴C]palmitic (C16:0) acid was lower in the soleus muscle and liver of ZDF rats vs. lean rats ($P < .05$). When administered orally to ZDF rats for 2 wk, the thiazolidinediones troglitazone (300 mg/kg) and KRP-297 (10 mg/kg) increased palmitic acid oxidn. in the soleus muscle of ZDF rats ($P < .05$). KRP-297, but not troglitazone, increased palmitic acid oxidn. in the liver of ZDF rats ($P < .05$), and both troglitazone and KRP-297 inhibited triglyceride accumulation in the skeletal muscle of ZDF rats. Hepatic triglyceride accumulation in ZDF rats was inhibited by KRP-297, but not by troglitazone. A redn. of fatty acid oxidn. in the liver of ZDF rats and an increase in response to KRP-297 were obsd. only when C16:0 and C18:0 fatty acids, not C8:0, were used as substrates. Thus, there were defects in fatty acid catabolic activity and triglyceride accumulation in the soleus muscle and liver of ZDF rats. These results indicate that KRP-297 has advantages over troglitazone in the amelioration of these lipid metabolic abnormalities in

L4 ANSWER 24 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)
 insulin resistance assocd. with obesity.
 IT 213252-19-8, KRP-297
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (tissue-specific actions of antidiabetic thiazolidinediones on reduced fatty acid oxidn. in muscle and liver in NIDDM/obesity)
 RN 213252-19-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



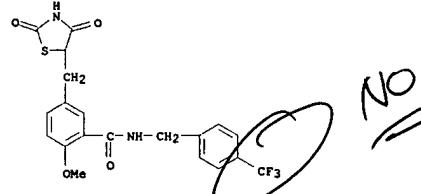
REFERENCE COUNT:
 FOR THIS
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 32 THERE ARE 32 CITED REFERENCES AVAILABLE
 RECORD. ALL CITATIONS AVAILABLE IN THE

L4 ANSWER 25 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 2000:190928 CAPLUS
 DOCUMENT NUMBER: 132:231969
 TITLE: Method for treating diabetes employing an aP2 inhibitor and combination
 INVENTOR(S): Robl, Jeffrey A.; Parker, Rex A.; Biller, Scott A.; Jamil, Haris; Jacobson, Bruce L.; Kodukula, Krishna
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA
 SOURCE: PCT Int. Appl., 55 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000015229	A1	20000323	WO 1999-US20946	19990913
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9963877	A1	20000403	AU 1999-63877	19990913
BR 9913833	A	20010529	BR 1999-13833	19990913
EP 1121129	A1	20010808	EP 1999-951438	19990913
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
NO 2001001351	A	20010511	NO 2001-1351	20010316
LT 4871	B	20011227	LT 2001-22	20010316
LT 4870	B	20011227	LT 2001-23	20010316
US 2002035064	A1	20020321	US 2001-905235	20010713
PRIORITY APPLN. INFO.: US 1998-100677P P 19980817				
			US 1999-390275	B1 19990907
			WO 1999-US20946	W 19990913

OTHER SOURCE(S): MARPAT 132:231969
 AB A method is provided for treating diabetes and related diseases, such as insulin resistance, obesity, hyperglycemia, hyperinsulinemia, elevated blood levels of free fatty acids or glycerol, hypertriglyceridemia, and esp. Type II diabetes, employing an adipocyte protein aP2 inhibitor or a

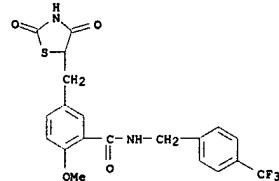
L4 ANSWER 25 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)
 such as metformin, glyburide, troglitazone and/or insulin.
 IT 213252-19-8, KRP 297
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (aP2 inhibitor and combination with another antidiabetic agent for treatment of diabetes and related diseases)
 RN 213252-19-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



NO
 2 THERE ARE 2 CITED REFERENCES AVAILABLE
 RECORD. ALL CITATIONS AVAILABLE IN THE
 RE FORMAT

L4 ANSWER 26 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1999:751167 CAPLUS
 DOCUMENT NUMBER: 132:44794
 TITLE: Amelioration by KRP-297, a new thiazolidinedione, of impaired glucose uptake in skeletal muscle from obese insulin-resistant animals
 AUTHOR(S): Murakami, Koji; Tsunoda, Masaki; Ide, Tomohiro; Ohashi, Mitsuo; Mochizuki, Toshiro
 CORPORATE SOURCE: Central Research Laboratories, Kyorin Pharmaceutical Co Ltd, Tochigi, Japan
 SOURCE: Metabolism, Clinical and Experimental (1999), 48(11), 1450-1454
 PUBLISHER: W. B. Saunders Co.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB We examd. the effect of KRP-297, a new thiazolidinedione deriv., on glucose uptake in the soleus muscle of two animal models of insulin resistance that show moderate (ob/ob mice) and severe (db/db mice) hyperglycemia. Insulin-stimulated 2-deoxyglucose (2DG) uptake in soleus muscle was 53.8% lower in ob/ob mice vs. lean mice ($P < .05$). When administered to ob/ob mice, KRP-297 (0.3 to 10 mg/kg) decreased plasma glucose and insulin levels and improved the impaired insulin-stimulated 2DG uptake in soleus muscle in a dose-dependent manner. Soleus muscle from db/db mice exhibited defects in both basal (35.0% decrease, $P < .01$) and insulin-stimulated (50.5% decrease, $P < .01$) 2DG uptake. These defects were improved by treatment with KRP-297 (0.3 to 10 mg/kg). Moreover, KRP-297 prevented severe hyperglycemia and the marked decrease in pancreatic insulin content in db/db mice. These results suggest that KRP-297 treatment is useful to prevent the development of diabetic syndromes in addn. to ameliorating the impaired glucose transport in skeletal muscle.
 IT 213252-19-8, KRP-297
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (thiazolidinedione deriv. KRP-297 amelioration of impaired glucose uptake in skeletal muscle from obese insulin-resistant animals)
 RN 213252-19-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)

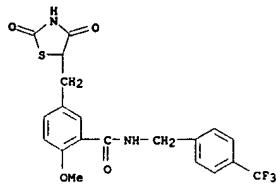
L4 ANSWER 26 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE
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L4 ANSWER 27 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1999:436161 CAPLUS
 DOCUMENT NUMBER: 131:238315
 TITLE: Evidence for direct binding of fatty acids and eicosanoids to human peroxisome
 proliferator-activated receptor .alpha.
 AUTHOR(S): Murakami, Koji; Ide, Tomohiro; Suzuki, Masahiro;
 CORPORATE SOURCE: Mochizuki, Toshiro; Kadokawa, Takashi
 Central Research Laboratories, Kyorin
 Co., Ltd., Tochigi, Japan
 SOURCE: Biochemical and Biophysical Research Communications
 (1999), 260(3), 609-613
 PUBLISHER: Academic Press
 DOCUMENT TYPE: CODEN: BBRCB9; ISSN: 0006-291X
 LANGUAGE: English
 AB The .alpha. isoform of peroxisome proliferator-activated receptor (PPAR)
 is activated by fatty acids, their metabolites, and the fibrate class of lipid-lowering agents. To test the ability of these activators to directly bind the ligand-binding domain of human PPAR.alpha., we performed a competitive binding assay using radiolabeled [³H]KRP-297, a known ligand for human PPAR.alpha.. Long-chain fatty acids and eicosanoids were even more potent ligands for human PPAR.alpha. than the hitherto most potent PPAR.alpha. ligand WY-14,643. Moreover, these natural ligands avidly activated this receptor in a transient transcriptional assay. This study provides the direct evidence that human PPAR.alpha. is activated through the direct binding of fatty acids and eicosanoids, as well as of a fibrate, to its ligand-binding domain. (c) 1999 Academic Press.
 IT 213252-19-8, KRP-297
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses) (direct binding of fatty acids and eicosanoids to human peroxisome proliferator-activated receptor .alpha.)
 RN 213252-19-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-trifluoromethyl)phenyl]methyl- (9CI) (CA INDEX NAME)

L4 ANSWER 27 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)



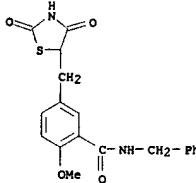
REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 28 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1999:188591 CAPLUS
 DOCUMENT NUMBER: 130:311725
 TITLE: (3-Substituted benzyl)thiazolidine-2,4-diones as structurally new antihyperglycemic agents
 AUTHOR(S): Nomura, Masahiro; Kinoshita, Susumu; Sato, Hiroya; Maeda, Toshiro; Murakami, Koji; Tsunoda, Masaki; Miyachi, Hiroyuki; Awano, Katuya
 CORPORATE SOURCE: Central Research Laboratories, Kyorin
 Pharmaceutical Co., Ltd., Tochigi, 329-0114, Japan
 SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(4), 533-538
 PUBLISHER: CODEN: BMCLB8; ISSN: 0960-894X
 DOCUMENT TYPE: Elsevier Science Ltd.
 LANGUAGE: Journal English
 GI

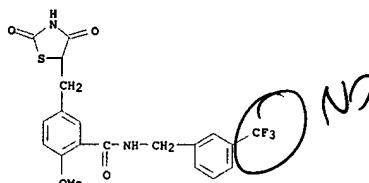
10/23

AB Title compds. I (R₁ = 4-tert-Bu, H, 4-Me, -MeO, 4-CF₃, etc.; R₂ = H, Et; R₃ = 6-MeO, 4-MeO, 2-MeO, 6-EtO, 6-OH, 6-F, etc.; m = 0-3; n = 0-2) were prepd. A structure-activity study of these compds. led to the identification of I (R₁ = CF₃, R₂ = H, R₃ = 6-MeO, m = n = 1) (KRP-297) as a candidate drug for the treatment of diabetes mellitus.
 IT 185808-38-28 185808-40-6P 185808-42-8P
 185808-45-18 185808-49-5P 185808-51-9P
 185808-62-2P 185808-63-3P 185808-64-4P
 185808-65-5P 185808-67-7P 185808-68-8P
 185808-70-2P 186312-06-7P 213252-19-8P,
 KRP-297 223508-01-4P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation) (prep. and antihyperglycemic activity of)
 RN 185808-38-2 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

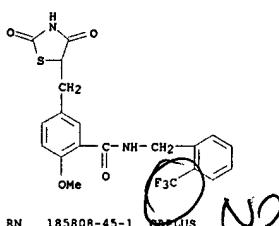
L4 ANSWER 28 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 185808-40-6 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(3-trifluoromethyl)phenyl]methyl- (9CI) (CA INDEX NAME)

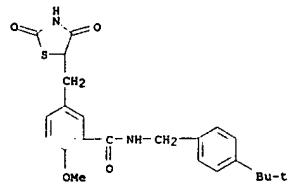


RN 185808-42-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(2-trifluoromethyl)phenyl]methyl- (9CI) (CA INDEX NAME)

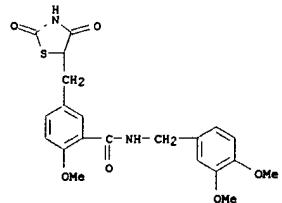


RN 185808-45-1 CAPLUS

L4 ANSWER 28 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)
 CN Benzamide, N-[{4-(1,1-dimethylethylphenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)

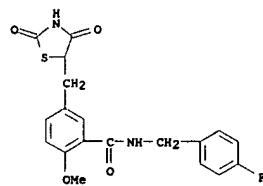


RN 185808-49-5 CAPLUS
 CN Benzamide, N-[{3,4-dimethoxyphenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)

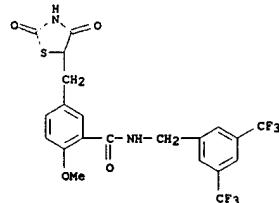


RN 185808-51-9 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-N-[(4-fluorophenyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)

L4 ANSWER 28 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)

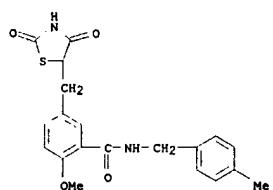


RN 185808-62-2 CAPLUS
 CN Benzamide, N-[{3,5-bis(trifluoromethyl)phenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)

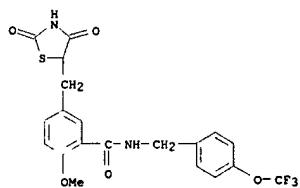


RN 185808-63-3 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-methylphenyl)methyl]- (9CI) (CA INDEX NAME)

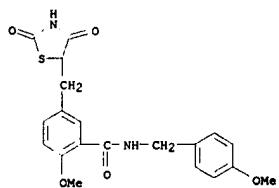
L4 ANSWER 28 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)



RN 185808-64-4 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethoxy)phenyl)methyl]- (9CI) (CA INDEX NAME)

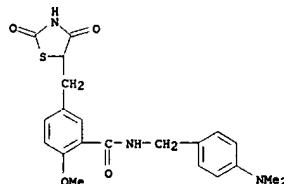


RN 185808-65-5 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

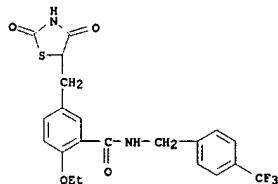


L4 ANSWER 28 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)

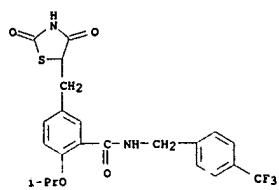
RN 185808-67-7 CAPLUS
 CN Benzamide, N-[(4-(dimethylamino)phenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)



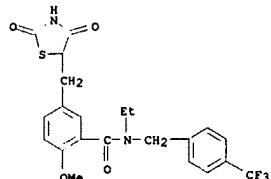
RN 185808-68-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-ethoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



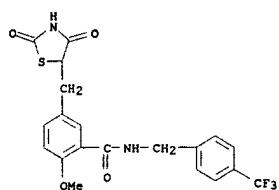
RN 185808-70-2 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-(1-methylethoxy)-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



RN 186312-86-7 CAPLUS
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-N-ethyl-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)

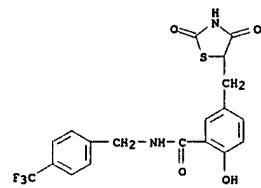


RN 213252-19-8 CAPLUS
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 29 OF 32 CAPLUS COPYRIGHT 2002 ACS
ACCESSION NUMBER: 1998:784882 CAPLUS
DOCUMENT NUMBER: 130:148506
TITLE: A novel insulin sensitizer acts as a coligand
for peroxisome proliferator-activated
receptor- α .
(PPAR- α) and PPAR- γ : effect of
metabolism in liver of Zucker fatty rats.
AUTHOR(S): Murakami, Koji; Tobe, Kazuyuki; Ide, Tomohiro;
Mochizuki, Toshiro; Ohashi, Mitsuhiro; Akanuma,
Yasuo;
CORPORATE SOURCE: Yazaki, Yoshio; Kadokawa, Takashi
of Third Department of Internal Medicine, Faculty
Medicine, University of Tokyo, Tokyo, 113,
Japan
SOURCE: Diabetes (1998), 47(12), 1841-1847
PUBLISHER: CODEN: DIABEZ; ISSN: 0012-1797
DOCUMENT TYPE: American Diabetes Association
LANGUAGE: Journal
AB We investigated the biol. activity of a novel thiazolidinedione
(TZD)
deriv., KRP-297, and the mol. basis of this activity. When
administered to obese Zucker fatty rats (obese rats) at 10 mg/kg for 2 wk,
KRP-297, unlike BRL-49653, restored reduced lipid oxidn. i.e., CO2 and
ketone body prodn. from [14C]palmitic acid, in the liver by 39% ($P < 0.05$) and
57% ($P < 0.01$), resp. KRP-297 was also significantly more effective than
BRL-49653 in the inhibition of enhanced lipogenesis and
triglyceride accumulation in the liver. To understand the mol. basis of the
biol. effects of KRP-297, we exmd. the effect on peroxisome
proliferator-activated receptor (PPAR) isoforms, which may play
key roles in lipid metab. Unlike classical TZD derivs., KRP-297 activated
both PPAR- α and PPAR- γ , with median effective concns. of
1.0 and 0.8 μ mol/L, resp. Moreover, radiolabeled [³H]KRP-297 bound
directly to PPAR- α and PPAR- γ , with dissociation constants of 228 and 326
nmol/L, resp. Concomitantly, KRP-297, but not BRL-49653, increased the
mRNA and the activity (1.5-fold [$P < 0.01$] and 1.8-fold [$P < 0.05$], resp.)
of acyl-CoA oxidase, which has been reported to be regulated by
PPAR- α , in the liver. By contrast, KRP-297 ($P < 0.05$) was less potent than

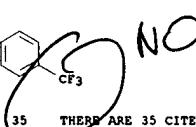
RN 223508-81-4 CAPLUS
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-hydroxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT:
FOR THIS
RE FORMAT

15 THERE ARE 15 CITED REFERENCES AVAILABLE
RECORD. ALL CITATIONS AVAILABLE IN THE

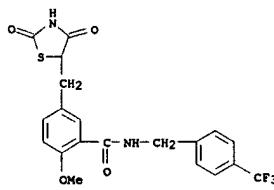
L4 ANSWER 29 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)
BRL-49653 ($P < 0.01$) in inducing the PPAR- γ -regulated aP2
gene mRNA expression in the adipose tissues. These results suggest that
PPAR- α agonism has a protective effect against abnormal
lipid metab.
in liver of obese rats.
IT 213252-19-8, KRP 297
RL: BAC (Biological activity or effector, except adverse); BSU
(Biological study, unclassified); THU (Therapeutic use); BIOL (Biological
study); USES
(Uses)
(effect of PPAR- α activation by insulin sensitizer,
thiazolidinedione deriv. KRP-297, on abnormal lipid metab. in
liver of
Zucker fatty rats)
RN 213252-19-8 CAPLUS
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)


REFERENCE COUNT:
FOR THIS
RE FORMAT

35 THERE ARE 35 CITED REFERENCES AVAILABLE
RECORD. ALL CITATIONS AVAILABLE IN THE

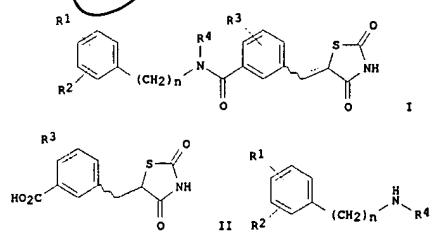
L4 ANSWER 30 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1998:421607 CAPLUS
 DOCUMENT NUMBER: 129:239719
 TITLE: Effects of PPAR.alpha. activation on liver lipid metabolism in Zucker fatty rats
 AUTHOR(S): Ide, Tomohiro; Murakami, Koji; Tobe, Kazuyuki; Mochizuki, Toshiro; Ohashi, Mitsuo; Akanuma, Yasuo; Kadowaki, Takashi; Yazaki, Yoshiro
 CORPORATE SOURCE: Cent. Res. Lab., Kyorin Pharm. Co., Ltd., Tochigi, 329-01, Japan
 SOURCE: Diabetes Frontier (1998), 9(3), 345-346 CODEN: DIFREZ; ISSN: 0915-6593
 PUBLISHER: Nodikaru Rebyusha
 DOCUMENT TYPE: Journal
 LANGUAGE: Japanese
 AB Oral administration of KRP-297 or BRL-49653 with high affinity to PPAR .alpha. to Zucker fatty (obese) rats and to control lean rats for 2 wk significantly lowered the blood glucose, insulin, triglyceride, and free fatty acid levels in the obese rats. KRP-297 and BRL-49653 also suppressed the increase in triglyceride accumulation and fatty acid biosynthesis activity in the liver of the obese rats as compared to the lean rats. In contrast, the markedly reduced activity of the hepatic acyl-CoA oxidase in the obese rats was markedly recovered by the administration. The results suggest that the activation of PPAR .alpha. by KRP-297 or BRL-49653 (ligand) might have inhibitory action on the hepatic triglyceride accumulation and lipid metab. abnormality in the obese rats.
 IT 213252-19-8, KRP 297
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (effects of PPAR.alpha. activation on liver lipid metab. in Zucker fatty rats)
 RN 213252-19-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)

L4 ANSWER 30 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)



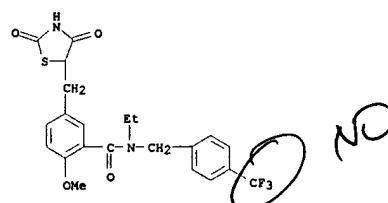
L4 ANSWER 31 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1997:116453 CAPLUS
 DOCUMENT NUMBER: 126:157499
 TITLE: Preparation of N-substituted dioxothiazolidylbenzamide derivatives as blood sugar lowering agents
 INVENTOR(S): Maeda, Toshio; Nomura, Masahiro; Awano, Katsuya; Kinoshita, Susumu; Sato, Hiroya; Murakami, Keiji; Tsunoda, Masaki
 PATENT ASSIGNEE(S): Kyorin Seiyaku Kk, Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.
 CODEN: JKKXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07333355	A2	19961217	JP 1995-159782	19950602
OTHER SOURCE(S): G1		MARPAT 126:157499		



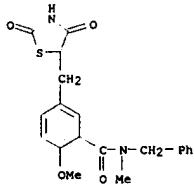
AB The title compds. (I: R1, R2 = H, Cl-4 alkyl, Cl-3 alkoxy, haloalkoxy, or haloalkyl, halo, OH, NO2, etc.; R3 = H, Cl-3 alkoxy, halo, OH; R4 = H, Cl-4 alkyl; dotted line = single or double bond; n = 0-2) are prep'd. by reacting benzoic acid derivs. (II: R3, dotted line = same as above) with amines (III: R1, R2, R4, n = same as above). I, possessing blood sugar and lipid lowering activities, are useful for diabetes mellitus and hyperlipemia. Thus, 5-(2,4-dioxo-5-thiazolidinyl-5-ylidene)methyl-2-methoxybenzoic acid was reacted with 4-tert-butylaniline in the presence

L4 ANSWER 31 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)
 of Et3N and NCP(O)(OEt)2 to give 99% I (R1 = 4-tert-BuC6H4, R3 = 2-MeO, R2 = R4 = H, dotted line = double bond, n = 0). I (R1 = R2 = 4-CF3, R3 = 6-MeO, R4 = Et, dotted line = single bond, n = 1) at 10 mg/kg showed 31% blood sugar lowering activity when tested on mouses p.o. in vivo. IT 186312-86-7P 186312-87-8P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prep'n. of N-substituted dioxothiazolidylbenzamide derivs. as blood sugar lowering agents)
 RN 186312-86-7 CAPLUS
 CN Benzamide,
 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



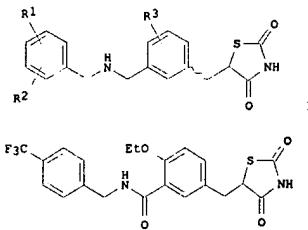
RN 186312-87-8 CAPLUS
 CN Benzamide,
 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-methyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)

10% generic
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genus.



L4 ANSWER 32 OF 32 CAPLUS COPYRIGHT 2002 ACS
 ACCESSION NUMBER: 1997-85180 CAPLUS
 DOCUMENT NUMBER: 126104076
 TITLE: Preparation of N-benzylidioxothiazolidylbenzamide derivatives as antidiabetics and hypolipemics
 INVENTOR(S): Maeda, Toshiro; Nomura, Masahiro; Awano,
 Katsuya; Kinoshita, Susumu; Sato, Hiroya; Murakami,
 Koji;
 PATENT ASSIGNEE(S): Tsunoda, Masaki
 Kyorin Pharmaceutical Co., Ltd., Japan; Maeda,
 Susumu; Nomura, Masahiro; Awano, Katsuya; Kinoshita,
 Sato, Hiroya; Murakami, Koji; Tsunoda, Masaki
 SOURCE: PCT Int. Appl., 40 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:
 12.5%

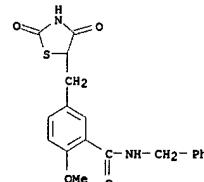
PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9638428	A1	19961205	WO 1996-JP1459	19960530
JP 09048771	A2	19970218	JP 1996-153139	19960524
JP 3144624	B2	20010312		
JP 2001139565	A2	20010522	JP 2000-350367	19960524
CA 2220698	AA	19961205	CA 1996-2220698	19960530
AU 9658446	A1	19961218	AU 1996-58446	19960530
AU 698896	B2	19981112		
EP 846693	A1	19980610	EP 1996-920002	19960530
EP 846693	B1	20020123		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, NL, SE, PT, IE, FI				
CN 1186489	A	19980701	CN 1996-194390	19960530
CN 1069901	B	20010822		
AT 212341	E	20020215	AT 1996-920002	19960530
TW 400328	B	20000801	TW 1996-85106554	19960601
US 6030990	A	20000229	US 1997-952672	19971202
US 6001862	A	19991214	US 1999-292955	19990416
US 6147101	A	20001114	US 2000-482268	20000113
CN 1336366	A	20020220	CN 2000-130138	20001017
PRIORITY APPLN. INFO.:			JP 1995-159781 A	19950602
			JP 1996-153139 A	19960524
			WO 1996-JP1459 W	19960530
OTHER SOURCE(S): MARPAT 126:104076				
GI				



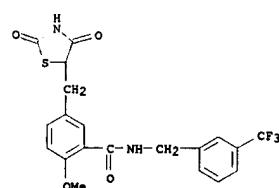
AB Novel N-benzylidioxothiazolidylbenzamide derivs. represented by general formula I [R1 and R2 are the same or different and each represents hydrogen, lower (C1-4) alkyl, lower (C1-3) alkoxy, lower haloalkyl, lower (C1-3) haloalkoxy, halogeno, hydroxy, nitro, amino optionally substituted by lower (C1-3) alkyl or a heterocycle, or R1 and R2 may be bonded to each other to form methylenedioxy; R3 represents lower (C1-3) alkoxy, hydroxy or halogeno; and the dotted line represents a double or single bond] are prep'd. The title compd. II at 10 mg/kg gave 37% decrease in blood sugar in obese mice.

IT 185808-38-28 185808-40-6P 185808-42-8P
 185808-45-18 185808-49-5P 185808-51-8P
 185808-62-28 185808-63-3P 185808-64-4P
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 185808-68-8P 185808-69-9P 185808-70-2P

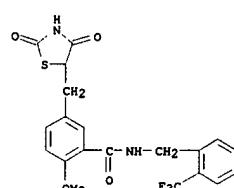
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses) (prep. of N-benzylidioxothiazolidylbenzamide derivs. as antidiabetics and hypolipemics)
 RN 185808-38-2 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



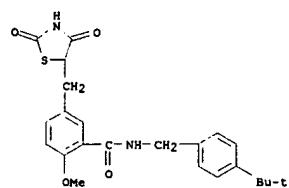
RN 185808-40-6 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(3-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



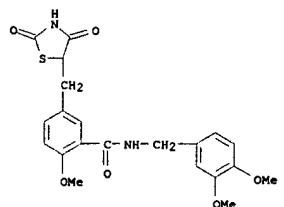
RN 185808-42-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(2-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 32 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)
 RN 185808-45-1 CAPLUS
 CN Benzamide, N-[(4-(1,1-dimethylethyl)phenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)

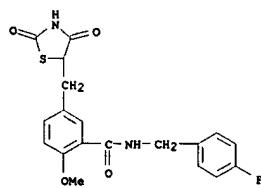


RN 185808-49-5 CAPLUS
 CN Benzamide, N-[(3,4-dimethoxyphenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)

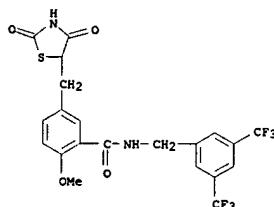


RN 185808-51-9 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-N-[(4-fluorophenyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)

L4 ANSWER 32 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)

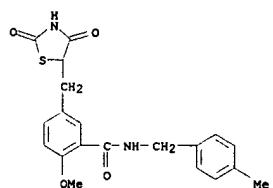


RN 185808-62-2 CAPLUS
 CN Benzamide, N-[(3,5-bis(trifluoromethyl)phenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)

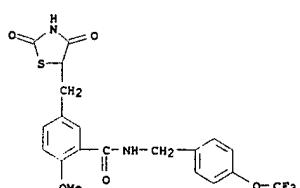


RN 185808-63-3 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-methylphenyl)methyl] (CA INDEX NAME)

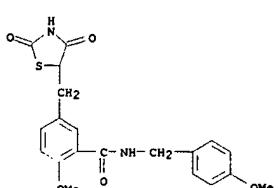
L4 ANSWER 32 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)



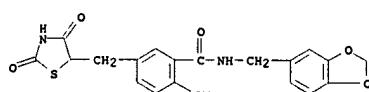
RN 185808-64-4 CAPLUS
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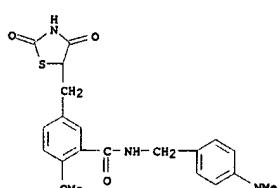
RN 185808-65-5 CAPLUS
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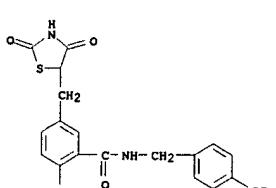
L4 ANSWER 32 OF 32 CAPLUS COPYRIGHT 2002 ACS (Continued)
 RN 185808-66-6 CAPLUS
 CN Benzamide, N-[(1,3-benzodioxol-5-ylmethyl)-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)



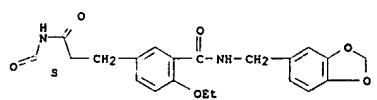
RN 185808-67-7 CAPLUS
 CN Benzamide, N-[(4-(dimethylamino)phenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)



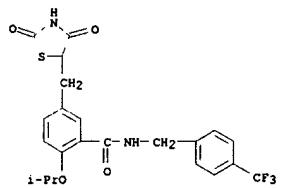
RN 185808-68-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-ethoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



RN 185808-69-9 CAPLUS
 CN Benzamide, N-[(1,3-benzodioxol-5-ylmethyl)-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-ethoxy- (9CI) (CA INDEX NAME)



RN 185808-70-2 CAPLUS
CN Benzamide,
S-(2,4-dioxo-5-thiazolidinyl)methyl)-2-(1-methylethoxy)-N-[(4-trifluoromethylphenyl)methyl]- (9CI) (CA INDEX NAME)



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SSSPTA1613SXW

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NEWS 6 Apr 22 Records from IP.com available in CAPLUS, HCAPLUS, and ZCAPLUS
NEWS 7 Apr 22 BIOSIS Gene Names now available in TOXCENTER
NEWS 8 Apr 22 Federal Research in Progress (FEDRIP) now available
NEWS 9 Jun 03 New e-mail delivery for search results now available
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NEWS 12 Jul 02 FOREGE no longer contains STANDARDS file segment
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saved answer sets no longer valid
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now available on STN
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NEWS 23 Sep 03 JAPIO has been reloaded and enhanced
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NEWS 25 Sep 16 CA Section Thesaurus available in CAPLUS and CA
NEWS 26 Oct 01 CASREACT Enriched with Reactions from 1907 to 1985
NEWS 27 Oct 21 EVENTLINE has been reloaded
NEWS 28 Oct 24 BEILSTEIN adds new search fields
NEWS 29 Oct 24 Nutraceuticals International (NUTRACEUT) now available on STN
NEWS 30 Oct 25 MEDLINE SDI run of October 8, 2002
NEWS 31 Nov 18 DKILIT has been renamed APOLLIT
NEWS 32 Nov 25 More calculated properties added to REGISTRY
NEWS 33 Dec 02 TIBKAT will be removed from STN

NEWS 34 Dec 04 CSA files on STN
 NEWS 35 Dec 17 PCTFULL now covers WP/PCT Applications from 1978 to date
 NEWS 36 Dec 17 TOXCENTER enhanced with additional content
 NEWS 37 Dec 17 Adis Clinical Trials Insight now available on STN
 NEWS 38 Dec 30 ISMPEC no longer available
 NEWS 39 Jan 21 NUTRACEUT offering one free connect hour in February 2003
 NEWS 40 Jan 21 PHARMAML offering one free connect hour in February 2003
 NEWS 41 Jan 29 Simultaneous left and right truncation added to COMPENDEX,
 ENERGY, INSPEC
 NEWS 42 Feb 13 CANCERLIT is no longer being updated
 NEWS 43 Feb 24 METADEX enhancements
 NEWS 44 Feb 24 PCTGEN now available on STN
 NEWS 45 Feb 24 TEMA now available on STN
 NEWS 46 Feb 26 NTIS now allows simultaneous left and right truncation
 NEWS 47 Feb 26 PCTFULL now contains images
 NEWS 48 Mar 04 SDI PACKAGE for monthly delivery of multifile SDI results
 NEWS 49 Mar 19 APOLLIT offering free connect time in April 2003
 NEWS 50 Mar 20 EVENTLINE will be removed from STN
 NEWS 51 Mar 24 PATDPAFULL now available on STN
 NEWS 52 Mar 24 Additional information for trade-named substances without
 structures available in REGISTRY
 NEWS 53 Mar 24 Indexing from 1957 to 1966 added to records in CA/CAPLUS

 NEWS EXPRESS January 6 CURRENT WINDOWS VERSION IS V6.01a,
 CURRENT MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
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DICTIONARY FILE UPDATES: 25 MAR 2003 HIGHEST RN 500688-79-9

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<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

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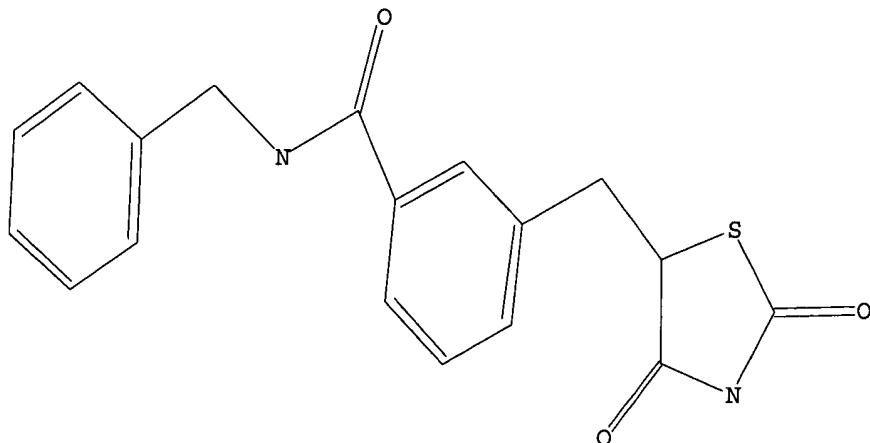
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L1 STRUCTURE UPLOADED

=> D

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

=> S L1 SSS SAM

SAMPLE SEARCH INITIATED 08:57:50 FILE 'REGISTRY'

SAMPLE SCREEN SEARCH COMPLETED - 13 TO ITERATE

100.0% PROCESSED 13 ITERATIONS
SEARCH TIME: 00.00.01

2 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
 BATCH **COMPLETE**
PROJECTED ITERATIONS: 44 TO 476
PROJECTED ANSWERS: 2 TO 124

L2 2 SEA SSS SAM L1

10049937

=> S L1 FULL
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100.0% PROCESSED 213 ITERATIONS 53 ANSWERS
SEARCH TIME: 00.00.01

L3 53 SEA SSS FUL L1

=> FIL CAPLUS
COST IN U.S. DOLLARS SINCE FILE TOTAL
FULL ESTIMATED COST ENTRY SESSION
148.15 148.36

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This file contains CAS Registry Numbers for easy and accurate substance identification.

=> S L3 FULL
L4 42 L3

=> D L4 1-42 IBIB ABS HITSTR

L4 ANSWER 1 OF 42 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:927185 CAPLUS
DOCUMENT NUMBER: 138:24716
TITLE: Preparation of azolecarboxylic acids useful as antidiabetic and antiobesity agents
INVENTOR(S): Cheng, Peter T.; Zhang, Hao; Hariharan, Narayanan
PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
SOURCE: PCT Int. Appl., 169 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

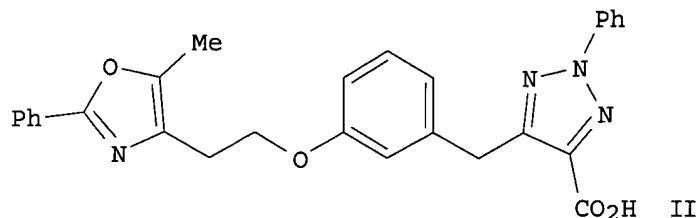
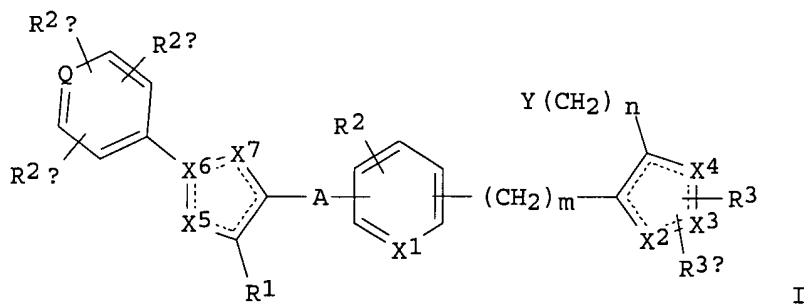
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|-------|-------|-----------------|-------|
| ----- | ----- | ----- | ----- | ----- |

WO 2002096358 A2 20021205 WO 2002-US16633 20020523
 W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
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 GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
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 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
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PRIORITY APPLN. INFO.: US 2001-294380P P 20010530

OTHER SOURCE(S): MARPAT 138:24716

GI



AB Title compds. [I; m, n = 0-2; Q = C, N; A = (CH₂)_x, (CH₂)_{x1}, (CH₂)_{x2}(CH₂)_{x3}; x = 1-5; x₁ = 2-5; x₂, x₃ = 0-5; .gtoreq. 1 of x₂, x₃ .noteq. 0; X₁ = CH, N; X₂, X₃, X₄, X₅, X₇ = C, N, O, S; in each of X₁-X₇, C may include CH; R₁ = H, alkyl; R₂ = H, alkyl, alkoxy, halo, (substituted) amino; R_{2a}, R_{2b} and R_{2c} = H, alkyl, alkoxy, halo, (substituted) amino; R₃, R_{3a} = H, alkyl, arylalkyl, aryloxycarbonyl, alkyloxycarbonyl, alkynyoxy carbonyl, alkenyoxy carbonyl, aryloxycarbonyl, arylcarbonyl, alkylcarbonyl, aryl, heteroaryl, alkyl(halo)aryloxycarbonyl, alkoxy(halo)aryloxycarbonyl, cycloalkylaryloxycarbonyl, cycloalkyloxyaryloxycarbonyl, cycloheteroalkyl, heteroarylcarbonyl, heteroarylheteroarylalkyl, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkoxycarbonylamino, aryloxycarbonylamino, heteroarylheteroarylcarbonyl, alkylsulfonyl, alkenylsulfonyl, heteroaryloxy carbonyl, cycloheteroalkyloxycarbonyl, heteroarylalkyl, aminocarbonyl, substituted aminocarbonyl, alkylaminocarbonyl, arylaminocarbonyl, aryloxyarylalkyl, alkynyoxy carbonyl, haloalkoxyarylloxycarbonyl, alkoxy carbonylaryloxycarbonyl, aryloxyarylloxycarbonyl, arylsulfinylarylcarbonyl, etc.; Y = CO₂R₄,

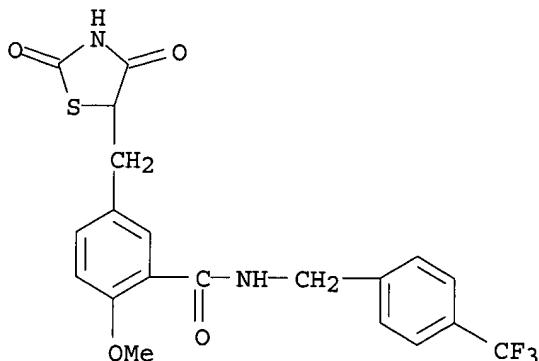
1-tetrazolyl, P(O)(OR_{4a})R₅, P(O)(OR_{4a})₂; R₄ = H, alkyl, prodrug ester; R_{4a} = H, prodrug ester; R₅ = alkyl, aryl; with provisos], were prepd. as simultaneous inhibitors of peroxisome proliferator activated receptor-.gamma. (PPAR.gamma.) and stimulators of peroxisome proliferator activated receptor-.alpha. (PPAR.alpha.). Thus, title compd. (II) (prepd. starting from Meldrum's acid 3-methoxyphenylacetyl chloride) bound to human PPAR.alpha. and to PPAR.gamma. ligand binding domains with IC₅₀ = 69 nM.

IT 213252-19-8, Krp297

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (coadministration; prepn. of azolecarboxylic acids useful as antidiabetic and antiobesity agents)

RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 2 OF 42 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:927184 CAPLUS

DOCUMENT NUMBER: 138:14048

TITLE: Preparation of oxazolyloxyphenylprolines and related compounds as antidiabetic and antiobesity agents.

INVENTOR(S): Cheng, Peter T.; Jeon, Yoon; Wang, Wei

PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA

SOURCE: PCT Int. Appl., 107 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

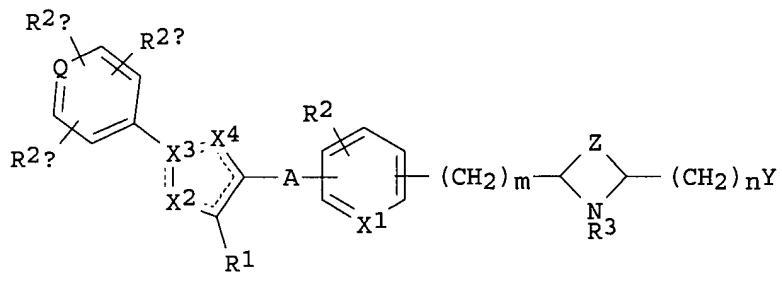
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
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| WO 2002096357 | A2 | 20021205 | WO 2002-US16628 | 20020523 |
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| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, | | | |

CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

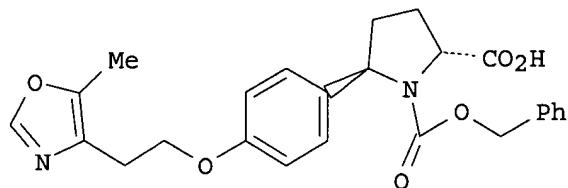
PRIORITY APPLN. INFO.: US 2001-294505P P 20010530

OTHER SOURCE(S): MARPAT 138:14048

GI



I



II

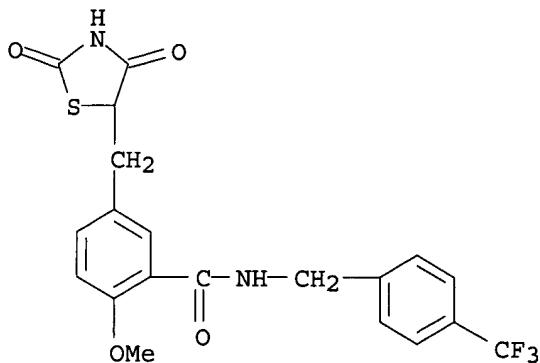
AB Title compds. [I; m, n = 0-2; Q = C, N; A = (CH₂)_x, (CH₂)_{x1}, with an alkenyl or alkynyl bond in the chain, (CH₂)_{x20}(CH₂)_{x3}; x = 1-5; x₁ = 2-5; x₂, x₃ = 0-5; provided that .gtoreq.1 of x₂ and x₃ .noteq. 0; X₁ = CH, N; X₂ = C, N, O, S; X₃ = C, N; X₄ = C, N, O, S provided that .gtoreq.1 of X₂, X₃, X₄ = N; in each of X₁-X₄, C may include CH; R₁ = H, alkyl; R₂ = H, alkyl, alkoxy, halo, (substituted) amino; R_{2a}, R_{2b} R_{2c} = H, alkyl, alkoxy, halo, (substituted) amino; R₃ = H, alkyl, arylalkyl, aryloxycarbonyl, alkylloxycarbonyl, alkynylloxycarbonyl, alkenyloxycarbonyl, arylcarbonyl, alkylcarbonyl, aryl, heteroaryl, cycloheteroalkyl, heteroarylcarbonyl, heteroarylheteroarylalkyl, alkylcarbonylamino, arylcarbonylamino, heteroarylcarbonylamino, alkoxy carbonylamino, aryloxycarbonylamino, heteroaryloxycarbonylamino, heteroaryl heteroarylcarbonyl, alkylsulfonyl, alkenylsulfonyl, heteroaryloxycarbonyl, cycloheteroalkyloxycarbonyl, aryloxyheteroarylalkyl, heteroarylalkyloxyarylalkyl, arylarylalkyl, arylalkenylarylalkyl, arylaminoarylalkyl, etc.; Y = CO₂R₄, 1-tetrazolyl, P(O)(OR_{4a})R₅, P(O)(OR_{4a})₂; R₄ = H, alkyl, prodrug ester; R_{4a} = H, prodrug ester; R₅ = alkyl, aryl; Z = (CH₂)_{x4}, (CH₂)_{x5}, (CH₂)_{x6}O(CH₂)_{x7}; x₄ = 1-5; x₅ = 2-5; x₆, x₇ = 0-4], were prep'd. as antidiabetic and antiobesity agents (no data). Thus, title compd. (II) was prep'd. in 6 steps.

IT 213252-19-8, KRP297

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(coadministration; prepn. of oxazolylethoxyphenylprolines and related
compds. as antidiabetic and antiobesity agents)

RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-[trifluoromethyl]phenyl)methyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 3 OF 42 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:889852 CAPLUS

DOCUMENT NUMBER: 137:346174

TITLE: Use of PPAR-.gamma.agonists for the prevention or treatment of diseases associated with IL-10 production

INVENTOR(S): Winiski, Anthony

PATENT ASSIGNEE(S): Novartis AG, Switz.

SOURCE: Brit. UK Pat. Appl., 14 pp.

CODEN: BAXXDU

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|-------|----------|-----------------|----------|
| ----- | ----- | ----- | ----- | ----- |
| GB 2373725 | A1 | 20021002 | GB 2001-8087 | 20010330 |

PRIORITY APPLN. INFO.: GB 2001-8087 20010330

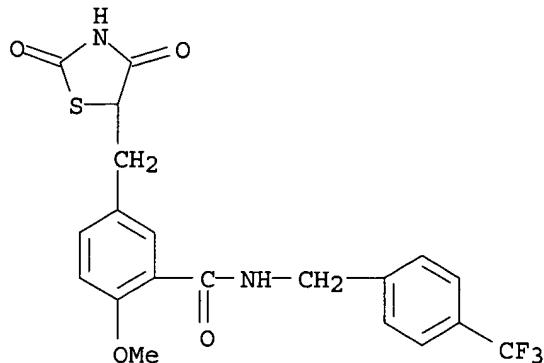
AB The invention discloses the use of PPAR-.gamma. agonists for the treatment of diseases related to the prodn. of Interleukin-10 (IL-10) like systemic lupus erythematosus, arthritis, cancer etc.

IT 213252-19-8, KRP-297

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of PPAR gamma agonist for prevention or treatment of diseases assocd. with IL-10 prodn.)

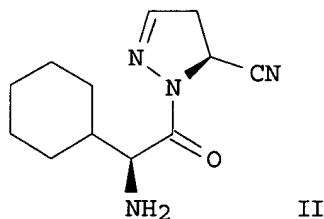
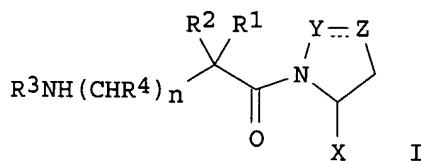
RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 4 OF 42 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2002:813924 CAPLUS
 DOCUMENT NUMBER: 137:311200
 TITLE: Preparation of 2,1-oxazoline and 1,2-pyrazoline-based inhibitors of dipeptidyl peptidase IV
 INVENTOR(S): Sulsky, Richard B.; Robl, Jeffrey A.
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
 SOURCE: PCT Int. Appl., 61 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|-------------------|-----------------|------------|
| WO 2002083128 | A1 | 20021024 | WO 2002-US10936 | 20020405 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2002183367 | A1 | 20021205 | US 2002-107279 | 20020326 |
| PRIORITY APPLN. INFO.: | | | US 2001-283438P | P 20010412 |
| OTHER SOURCE(S): | | MARPAT 137:311200 | | |
| GI | | | | |



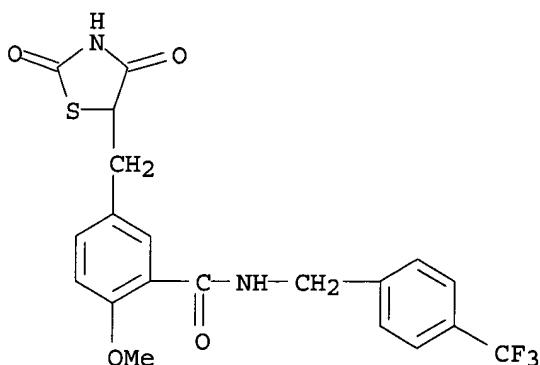
AB The invention describes dipeptidyl peptidase IV (DP 4) inhibiting compds. I [n is 0 or 1; X is H or CN; Y is N, NH or O; Z is CH₂ when Y is O or NH, with Y-Z forming a single bond, and Z is CH when Y is N, with Y-Z forming a double bond; R₁-R₄ = H, alkyl, alkenyl, alkynyl, cycloalkyl, cycloalkylalkyl, bicycloalkyl, bicycloalkylalkyl, alkylthioalkyl, arylalkylthioalkyl, cycloalkenyl, aryl, aralkyl, heteroaryl, heteroarylalkyl, cycloheteroalkyl or cycloheteroalkylalkyl, which may be substituted; R₁ may combine with R₃ or R₄ to form a ring (CR₅R₆)₂₋₆ or (CR₇R₈)₃₋₆, resp., where R₅-R₈ = H, OH, alkoxy, alkyl, aryl, etc.] and their pharmaceutically-acceptable salts or prodrug esters. A method is also provided for treating diabetes and related diseases, employing a DP 4 inhibitor I, optionally in combination with other therapeutic agents, including an antidiabetic, hypolipidemic, or anti-obesity agent. Thus, coupling of sultam-protected 1,2-pyrazoline-3-carboxamide with (S)-N-(tert-butoxycarbonyl)cyclohexylglycine (HOAt, Et₃N, and EDAC in CH₂Cl₂), followed by sultam cleavage with methanolic ammonia, amide conversion to nitrile using imidazole, and deprotection, afforded II.TFA.

IT 213252-19-8, KRP297

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antidiabetic agent; prepn. of oxazoline and pyrazoline-based
inhibitors of dipeptidyl peptidase IV)

RN 213252-19-8 CAPLUS

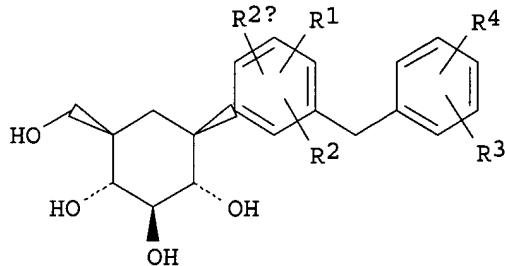
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 5 OF 42 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2002:813874 CAPLUS
 DOCUMENT NUMBER: 137:311199
 TITLE: Amino acid complexes of C-aryl glucosides for treatment of diabetes
 INVENTOR(S): Gougoutas, Jack Z.
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
 SOURCE: PCT Int. Appl., 80 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|--|-----------------|------------|
| WO 2002083066 | A2 | 20021024 | WO 2002-US11066 | 20020408 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | |
| PRIORITY APPLN. INFO.: | | | US 2001-283097P | P 20010411 |
| OTHER SOURCE(S): | | MARPAT 137:311199 | | |
| GI | | | | |



AB Cryst. complexes are obtained from 1:1 or 2:1 mixts. of either the (D) or (L) enantiomer of natural amino acids and compds. of formula I [R1, R2, R2a = H, OH, OR5, alkyl, OCF2, OCF3, SR5a, halogen; R3, R4 = H, OH, OR5b, alkyl, cycloalkyl, CF3, OCHF2, OCF3, halogen, CONR6R6a, CO2R5c, CO2H, COR6b, CH(OH)R6c, CH(OR5d)R6d, CN, NHCOR5e, NHSO2R5f, NHSO2-aryl, SR5g, SOR5h, SO2R5i, or a five, six or seven membered heterocycle which may contain 1 to 4 heteroatoms (N, O, S, SO, and/or SO2), or R3 and R4 together with the carbons to which they are attached form an annelated five, six or seven membered carbocycle or heterocycle which may contain 1 to 4 heteroatoms in the ring; R5, R5a-R5i are independently alkyl; R6,

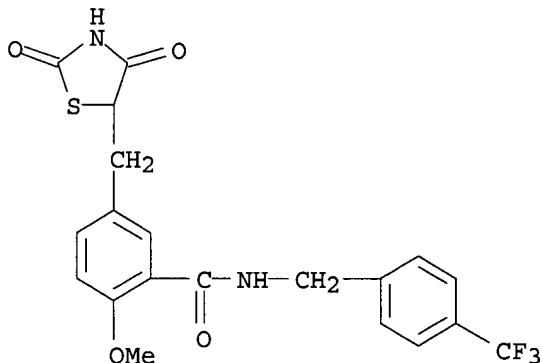
R6a-R6d are independently H, alkyl, aryl, alkylaryl or cycloalkyl, or NR6R6a form an annelated five, six or seven membered heterocycle which may contain 1 to 4 heteroatoms in the ring]. A method is also provided for treating diabetes and related diseases employing an SGLT2 (sodium dependent glucose transporters found in the intestine and kidney) inhibiting amt. of the above complex alone or in combination with another antidiabetic agent or other therapeutic agent. Thus, I (R1 = 4-Me, R4 = 4-OCHF₂, R2, R2a, R3 = H) was prep'd. by a multistep procedure starting from o-toluic acid, anisole, 2,3,4,6-tetra-O-benzyl-.beta.-D-glucolactone, and CHF₂Cl and treated with L-phenylalanine to form the cryst. 1:1 complex.

IT 213252-19-8, KRP297

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of amino acid/C-aryl glucoside complexes for treatment of diabetes and related diseases)

RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 6 OF 42 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:793435 CAPLUS

DOCUMENT NUMBER: 137:289021

TITLE: Combination therapy comprising glucose reabsorption inhibitors and PPAR modulators

INVENTOR(S): Bussolari, Jacqueline C.; Chen, Xiaoli; Conway, Bruce R.; Demarest, Keith T.; Ross, Hamish N. M.; Severino, Rafael

PATENT ASSIGNEE(S): Ortho McNeil Pharmaceutical, Inc., USA

SOURCE: PCT Int. Appl., 86 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|---|----------|-----------------|----------|
| WO 2002080936 | A1 | 20021017 | WO 2002-US10538 | 20020403 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, | | | |

PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
 UA, UG, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
 CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
 BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2003045553 A1 20030306 US 2002-115827 20020403

PRIORITY APPLN. INFO.: US 2001-281429P P 20010404

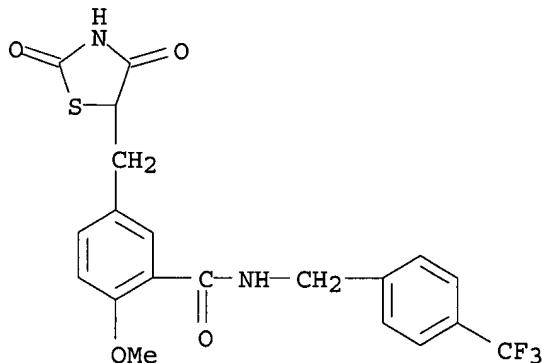
AB Combination therapy comprising PPAR modulators and glucose reabsorption inhibitors useful for the treatment of diabetes and Syndrome X are disclosed.

IT 213252-19-8, KRP-297

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (combination therapy comprising glucose reabsorption inhibitors and PPAR modulators)

RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 7 OF 42 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:736927 CAPLUS

DOCUMENT NUMBER: 137:247879

TITLE: Preparation of antidiabetic agents C-aryl glucoside as human SGLT2 inhibitors

INVENTOR(S): Ellsworth, Bruce; Washburn, William N.; Sher, Philip M.; Wu, Gang; Meng, Wei

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 17 pp., Cont.-in-part of U.S. 6,414,126.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

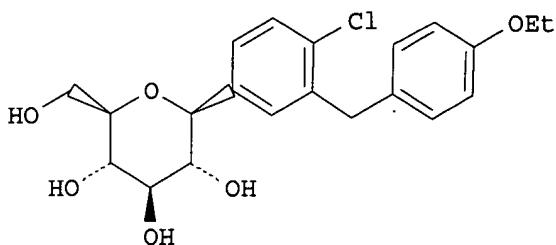
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| US 2002137903 | A1 | 20020926 | US 2002-151436 | 20020520 |
| US 6515117 | B2 | 20030204 | | |
| US 6414126 | B1 | 20020702 | US 2000-679027 | 20001004 |

PRIORITY APPLN. INFO.:

US 1999-158773P P 19991012
 US 2000-194615P P 20000405
 US 2000-679027 A2 20001004

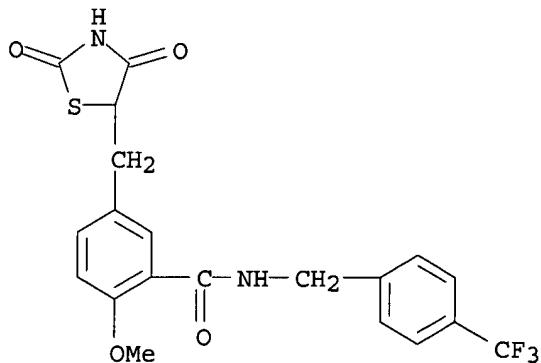
GI



AB An SGLT2 inhibiting compd. is provided having the formula I method is also provided for treating diabetes and related diseases employing an SGLT2 inhibiting amt. of the above compd. alone or in combination with another antidiabetic agent or other therapeutic agent (no data). 1A pharmaceutical combination comprising an SGLT2 inhibitor compd. and an antidiabetic agent other than an SGLT2 inhibitor, for treating the complications of diabetes, an anti-obesity agent, an antihypertensive agent, an antiplatelet agent, an antiatherosclerotic agent, and/or a lipid-lowering agent (no data). A method for treating or delaying the progression or onset of diabetes, diabetic retinopathy, diabetic neuropathy, diabetic nephropathy, delayed wound healing, insulin resistance, hyperglycemia, hyperinsulinemia, elevated blood levels of fatty acids or glycerol, hyperlipidemia, obesity, hypertriglyceridemia, Syndrome X, diabetic complications, atherosclerosis or hypertension, or for increasing high d. lipoprotein levels, which comprises administering to a mammalian species in need of treatment a therapeutically effective amt. of a compd (no data).

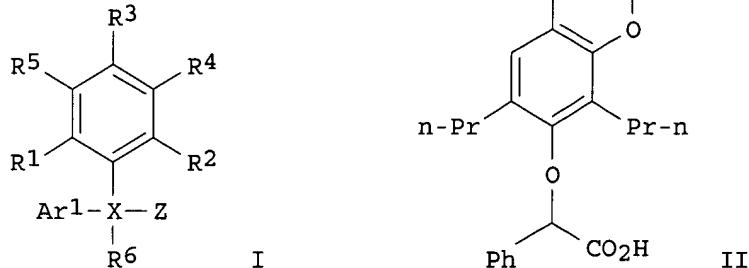
IT 213252-19-8, KRP297

RL: BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (prepn. of antidiabetic agents C-aryl glucosides as human SGLT2 inhibitors)

RN 213252-19-8 CAPLUS**CN** Benzamide, 5-[{(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-trifluoromethyl)phenyl]methyl- (9CI) (CA INDEX NAME)

L4 ANSWER 8 OF 42 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2002:637483 CAPLUS
 DOCUMENT NUMBER: 137:185311
 TITLE: Preparation of 2-aryloxy-2-arylalkanoic acids for diabetes and lipid disorders
 INVENTOR(S): Adams, Alan D.; Jones, A. Brian; Berger, Joel P.; Dropinski, James F.; Elbrecht, Alexander; Liu, Kun; Macnaul, Karen Lamb; Shi, Guo-qiang; Von, Langen Derek J.; Zhou, Gaochao
 PATENT ASSIGNEE(S): Merck & Co., Inc., USA
 SOURCE: PCT Int. Appl., 157 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|-------------------|-----------------|------------|
| WO 2002064094 | A2 | 20020822 | WO 2002-US4680 | 20020205 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRIORITY APPLN. INFO.: | | | US 2001-267809P | P 20010209 |
| OTHER SOURCE(S): | | MARPAT 137:185311 | | |
| GI | | | | |



AB Title compds. I [R₁ = halo, alkyl, alkoxy; R₂ = alkyl, alicyclic; R₃ = alkyl, aryl, alicyclic, heterocycle, etc.; R₄ = H, OH, alkoxy, aryloxy, halo or R₃-4 may be joined together to yield 5- or 6-membered heterocycle; R₅ = H, halo; R₆ = H, halo, CH₃, CF₃; Ar¹ = Ph, thienyl, thiazolyl, oxazolyl, pyridyl; X = O, S; Z = COOH, tetrazole, carboxamide] were prep'd. For instance, 2,4-dipropylresorcinol was converted to 2,4-dihydroxy-3,5-dipropyl-.alpha..alpha..-trifluoroacetophenone (CH₂Cl₂, TFAA,

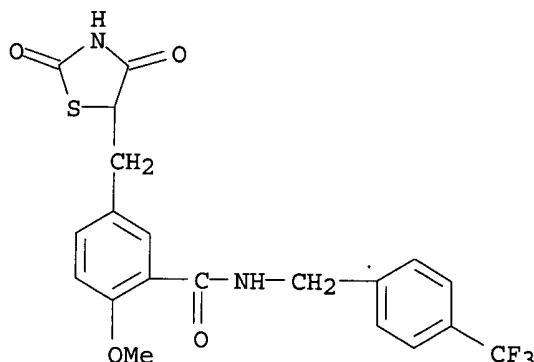
AlCl₃) and subsequently treated with i. hydroxylamine.bul.HCl, MeOH, reflux; ii. Ac₂O; iii. pyridine, reflux which afforded 5,7-dipropyl-6-hydroxy-3-trifluoromethyl-1,2-benzisoxazole. The benzisoxazole was reacted with Me 2-bromo-2-phenylacetate (DMF, Cs₂CO₃) and the product saponified to give II. I are potent agonists of the peroxisome proliferator activated receptor and are useful in the treatment of non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR-.alpha. and/or PPAR-.gamma. mediated diseases.

IT 213252-19-8, KRP-297

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses) (combination pharmaceutical; prepn. of 2-aryloxy-2-arylalkanoic acids for diabetes and lipid disorders)

RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl] - (9CI) (CA INDEX NAME)



L4 ANSWER 9 OF 42 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:594636 CAPLUS
 DOCUMENT NUMBER: 137:135097
 TITLE: Acyl sulfamides for treatment of obesity, diabetes and lipid disorders
 INVENTOR(S): Jones, A. Brian; Acton, John J., III
 PATENT ASSIGNEE(S): Merck & Co., Inc., USA
 SOURCE: PCT Int. Appl., 64 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2002060388 | A2 | 20020808 | WO 2002-US3119 | 20020125 |
| WO 2002060388 | A3 | 20030227 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2001-264955P P 20010130

OTHER SOURCE(S): MARPAT 137:135097

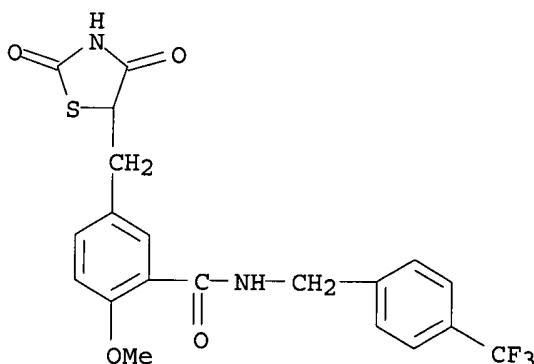
AB A class of acyl sulfamides comprises compds. that are potent ligands for PPAR. γ . receptors and generally have antagonist or partial agonist activity. The compds. may be useful in the treatment, control or prevention of obesity, non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, vascular restenosis, inflammation, and other PPAR. γ . receptor-mediated diseases, disorders and conditions, alone or in combination with one or more other compds. Other compds. are selected from insulin sensitizers, insulin or insulin mimetics, sulfonylureas, .alpha.-glucosidase inhibitors, cholesterol lowering agents, PPAR. δ . agonists, antidiabetic compds., an ileal bile acid transporter inhibitor, and agents intended for use in inflammatory conditions such as aspirin, nonsteroidal anti-inflammatory drugs, glucocorticoids, azulfidine, and cyclooxygenase-2 selective inhibitors.

IT 213252-19-8, KRP-297

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(acyl sulfamides and other drugs for treatment of metabolic disorders
mediated by PPAR. γ . receptors)

RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-
(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 10 OF 42 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:575765 CAPLUS

DOCUMENT NUMBER: 137:140435

TITLE: Benzopyrancarboxylic acid derivatives with PPAR
agonist activity for the treatment of diabetes and
lipid disorders, and their preparation, pharmaceutical
compositions, and use

INVENTOR(S): Sahoo, Soumya P.; Koyama, Hiroo; Miller, Daniel J.;
Boueres, Julia K.; Desai, Ranjit C.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 42 pp.

CODEN: USXXCO

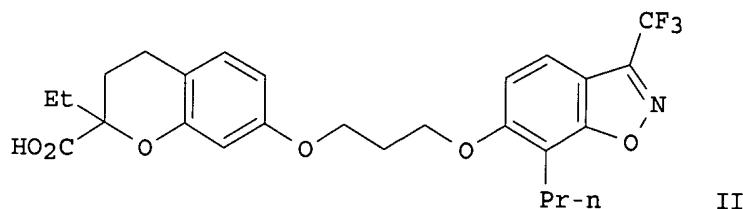
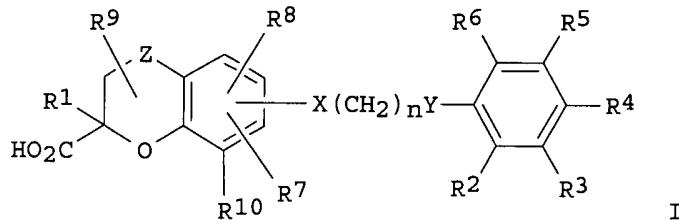
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|-------------------|-----------------|------------|
| US 2002103242 | A1 | 20020801 | US 2001-21667 | 20011029 |
| WO 2002060434 | A2 | 20020808 | WO 2001-US49501 | 20011026 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS,
LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT,
RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US,
UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| PRIORITY APPLN. INFO.: | | | US 2000-244698P | P 20001031 |
| OTHER SOURCE(S): | | MARPAT 137:140435 | | |
| GI | | | | |



AB A class of benzopyrancarboxylic acid derivs. is disclosed, which comprises compds. that are potent agonists (no data) of peroxisome proliferator activated receptors (PPAR) alpha and/or gamma, and are therefore useful in the treatment, control, or prevention of non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR alpha and/or gamma mediated diseases, disorders and conditions. In particular, compds. I and their pharmaceutically acceptable salts and/or prodrugs are disclosed [wherein: Z = CH₂, CO; R₁ = H, OH, halo, (un)substituted alk(en/yn)yl, alk(en/yn)yloxy, or aryl; or R₁ forms (un)substituted cyclopropane fusion to adjacent C atom; X, Y = O, S, SO, SO₂, CH₂, (un)substituted NH; n = 1-6; R₄ = (un)substituted benzoheterocyclyl, cycloalkyl, heterocyclyl, cycloalkyloxy, halo, OH or derivs., alk(en/yn)yl, alk(en/yn)yloxy, or aryl, etc.; other R groups = H, halo, OH, (un)substituted alk(en/yn)yl, alk(en/yn)yloxy, aryl, aryloxy, aroyl, etc.; or R₃R₄ or R₄R₅ = (un)substituted 5- or 6-membered heterocyclic ring]. A list of 29 compds.

is claimed, and their prepn. is described. For example, Et 7-hydroxy-4-oxo-4H-chromene-2-carboxylate underwent a sequence of: (1) complete hydrogenation of the enone (98%), (2) etherification of the alc. with PhCH₂O(CH₂)₃Br (66%), (3) alpha ethylation of the ester (70%), (4) hydrogenolytic debenzylolation (100%), (5) conversion of the resultant alc. to a bromide (96%), (6) etherification of the bromide with 3-(trifluoromethyl)-7-propyl-6-hydroxybenz[4,5]isoxazole (85%), and (7) alk. hydrolysis (100%), to give title compd. II. PPAR binding assays using human recombinant PPAR are described without data.

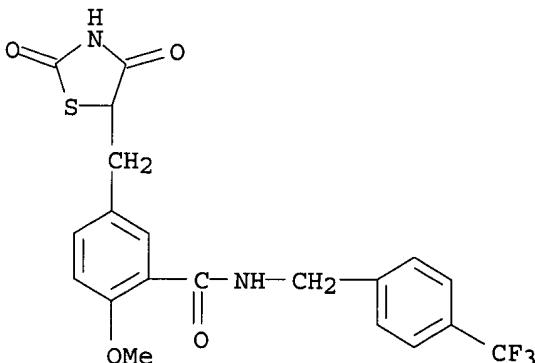
Co-administration of compds. I with a variety of other drug categories, including a no. of specific drugs, is claimed.

IT 213252-19-8, KRP-297

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic compns. also contg.; prepn. of benzopyrancarboxylic acid derivs. as PPAR agonists for treatment of diabetes and lipid disorders)

RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 11 OF 42 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:540258 CAPLUS

DOCUMENT NUMBER: 137:109267

TITLE: Preparation of benzoxepinopyridines as HMG-CoA reductase inhibitors

INVENTOR(S): Robl, Jeffrey A.; Chen, Bang-chi; Sun, Chong-qing

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 42 pp., Cont.-in-part of U.S. Ser. No. 875,155.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2002094977 | A1 | 20020718 | US 2001-7407 | 20011204 |
| US 2002013334 | A1 | 20020131 | US 2001-875155 | 20010606 |
| PRIORITY APPLN. INFO.: | | | US 2000-211595P | P 20000615 |
| | | | US 2001-875155 | A2 20010606 |

OTHER SOURCE(S): MARPAT 137:109267

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [X = O, S, SO, SO₂, NR₇; Z = HOCHCH₂CH(OH)CH₂CO₂R₃, 4-hydroxy-2-oxopyran-6-yl, etc.; n = 0, 1; R₁, R₂ = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R₃ = H, alkyl, metal ion; R₄ = H, halo, CF₃, etc.; R₇ = H, alkyl, aryl, alkanoyl, aroyl, alkoxycarbonyl, etc.; R₉, R₁₀ = H, alkyl], were prep'd. as HMG CoA reductase inhibitors active in inhibiting cholesterol biosynthesis, modulating blood serum lipids such as lowering LDL cholesterol and/or increasing HDL cholesterol, and treating hyperlipidemia, hypercholesterolemia, hypertriglyceridemia and atherosclerosis (no data). A multistep synthesis of II is reported.

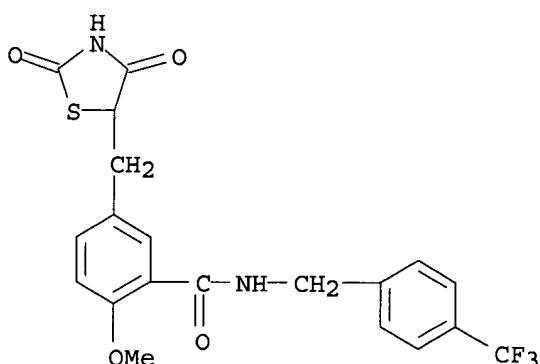
IT 213252-19-8, KRP297

RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(coadministered agents; prepn. of benzoxepinopyridines as HMG-CoA reductase inhibitors for treatment of hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, and other disorders)

RN 213252-19-8 CAPPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]-(9CI) (CA INDEX NAME)



L4 ANSWER 12 OF 42 CAPPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:504648 CAPPLUS

DOCUMENT NUMBER: 137:83637

TITLE: Medicinal compositions containing diuretic and insulin resistance-improving agent

INVENTOR(S): Takaoka, Masaya; Araki, Kazushi; Kanda, Shoichi

PATENT ASSIGNEE(S): Sankyo Company, Limited, Japan

SOURCE: PCT Int. Appl., 183 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.

KIND DATE

APPLICATION NO. DATE

 WO 2002051441 A1 20020704 WO 2001-JP11296 20011221
 W: AU, BR, CA, CN, CO, CZ, HU, ID, IL, IN, KR, MX, NO, NZ, PH, PL,
 RU, SG, SK, US, VN, ZA
 RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
 PT, SE, TR
 JP 2002255854 A2 20020911 JP 2001-386861 20011220
 PRIORITY APPLN. INFO.: JP 2000-394424 A 20001226

OTHER SOURCE(S) : MARPAT 137:83637

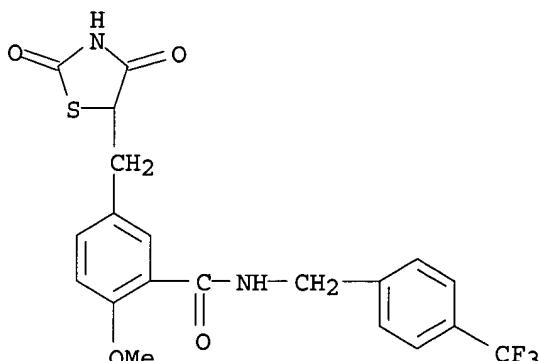
AB Disclosed are medicinal compns. contg. a diuretic and an insulin resistance-improving agent whereby side effects assocg. the administration of an insulin resistance-improving agent (for example, megalocardia, edema, body fluid retention, pleural effusion) can be prevented or treated. Oral administration of furosemide prevented increases of heart wt. and blood plasma, and edema due to administration of 5-[4-(6-methoxy-1-methyl-1H-benzimidazol-2-ylmethoxy)benzyl]thiazolidine-2,4-dione hydrochloride.

IT 213252-19-8, KRP-297

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (medicinal compns. contg. diuretics and insulin resistance-improving agents)

RN 213252-19-8 CAPLUS

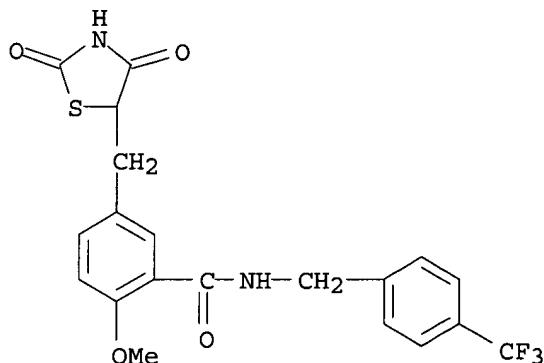
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 13 OF 42 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2002:409256 CAPLUS
 DOCUMENT NUMBER: 137:735
 TITLE: Methods and compositions for treatment of diabetes and related conditions via gene therapy
 INVENTOR(S): Caplan, Shari L.; Boettcher, Brian R.; Slosberg, Eric D.; Connelly, Sheila; Kaleko, Michael; Desai, Urvi J.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 42 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--|----------|-------------------|----------|
| US 2002065239 | A1 | 20020530 | US 2001-808457 | 20010314 |
| PRIORITY APPLN. INFO.: | | | US 2000-266328P P | 20000315 |
| AB Methods and compns. are disclosed for the treatment of diabetes, obesity and diabetic-related conditions. The methods include gene therapy based administration of a therapeutically effective amt. of vectors encoding the following: glucokinase regulatory protein alone or co-administered with glucokinase or with metab. modifying proteins; glucokinase co-administered with metab. modifying proteins; or glucokinase regulatory protein co-administered with glucokinase in combination with metab. modifying proteins, to a diabetic patient. The metab. modifying proteins include UCP2, UCP3, PPAR.alpha., OB-Rb, GLP-1 and GLP-1 analogs (administered via vector or directly as a peptide). Preferred examples of GLP-1 analogs include GLP-1-Gly8, Extendin-4 and the "Black Widow" chimeric GLP-1 analog. Addnl., PPAR.alpha. ligands and DPP-IV inhibitors may be co-administered with the above. | | | | |
| IT 213252-19-8, KRP-297 | RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gene therapy for treatment of diabetes and related conditions) | | | |
| RN 213252-19-8 CAPLUS | | | | |
| CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME) | | | | |

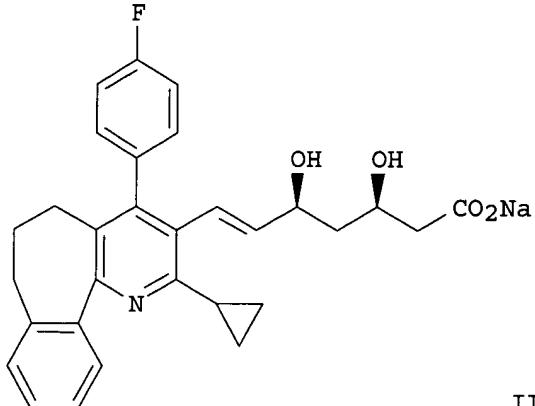
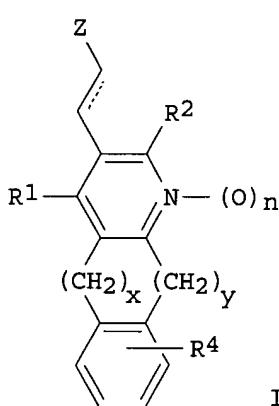


L4 ANSWER 14 OF 42 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2002:392237 CAPLUS
 DOCUMENT NUMBER: 136:401651
 TITLE: Preparation of fused pyridine derivatives as HMG-CoA reductase inhibitors
 INVENTOR(S): Robl, Jeffrey A.; Chen, Bang-Chi; Sun, Chong-Qing
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 46 pp., Cont.-in-part of U.S.
 Ser. No. 875,218.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

| | | | | |
|------------------------|----|----------|-----------------|-------------|
| US 2002061901 | A1 | 20020523 | US 2001-8154 | 20011204 |
| US 2002028826 | A1 | 20020307 | US 2001-875218 | 20010606 |
| PRIORITY APPLN. INFO.: | | | US 2000-211594P | P 20000615 |
| | | | US 2001-875218 | A2 20010606 |

OTHER SOURCE(S) : MARPAT 136:401651
GI



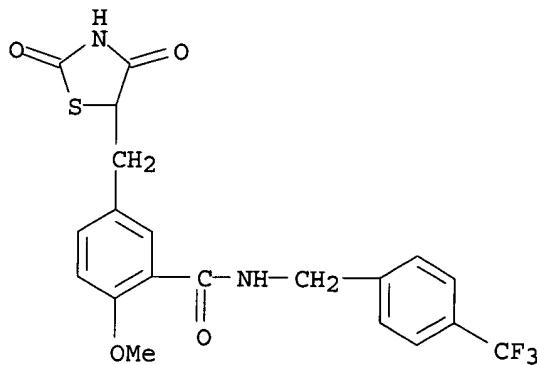
AB The title compds. I and their pharmaceutically acceptable salts, esters, prodrug esters, and stereoisomers are claimed [wherein: Z = CH(OH)CH₂CR₇(OH)CH₂CO₂R₃ or corresponding pyranone lactone derivs.; n = 0, 1; x = 0, 1, 2, 3, or 4; y = 0, 1, 2, 3 or 4, provided that at least one of x and y is other than 0; and optionally one or more carbons of (CH₂)_x and/or (CH₂)_y together with addnl. carbons form a 3 to 7 membered spirocyclic ring; R₁, R₂ = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R₃ = H or lower alkyl; R₄ = H, halo, CF₃, OH, alkyl, alkoxy, CO₂H, (un)substituted NH₂, cyano, (un)substituted CONH₂, etc.; R₇ = H, alkyl]. The compds. are HMG-CoA reductase inhibitors, and are active in inhibiting cholesterol biosynthesis and modulating blood serum lipids, for example, lowering LDL cholesterol and/or increasing HDL cholesterol (no data). I are thus useful in treating hyperlipidemia and dyslipidemia, in hormone replacement therapy, and in treating hypercholesterolemia, hypertriglyceridemia and atherosclerosis, as well as Alzheimer's disease and osteoporosis. Preps. of several compds. are described. For instance, a multistep synthesis of fused pyridine deriv. II is reported. Compds. I may be used in a manner similar to atorvastatin, pravastatin, simvastatin, etc. Combinations of compds. I with various other drugs are claimed, the latter being specified as certain pharmacol. classes, as inhibitors of specific enzymes, as (ant)agonists of specific receptors, and as numerous named drugs.

IT 213252-19-8, KRP297

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic compns. also contg.; prepn. of fused pyridine derivs. as HMG-CoA reductase inhibitors)

RN 213252-19-8 CAPLUS

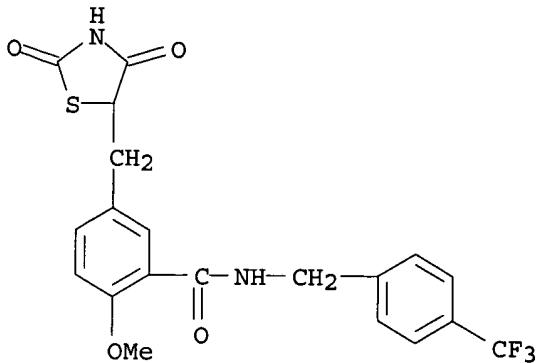
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 15 OF 42 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2002:142553 CAPLUS
 DOCUMENT NUMBER: 136:177969
 TITLE: Medicinal compositions containing PPAR.gamma. agonists and RXR agonists for preventing and treating cancer
 INVENTOR(S): Kurakata, Shinichi; Fujiwara, Kosaku; Shimazaki, Naomi; Fujita, Takashi
 PATENT ASSIGNEE(S): Sankyo Company, Limited, Japan
 SOURCE: PCT Int. Appl., 40 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2002013864 | A1 | 20020221 | WO 2001-JP7037 | 20010815 |
| W: AU, BR, CA, CN, CO, CZ, HU, ID, IL, IN, KR, MX, NO, NZ, PL, RU, SG, SK, US, ZA | | | | |
| RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR | | | | |
| JP 2002128700 | A2 | 20020509 | JP 2001-241740 | 20010809 |
| AU 2001078738 | A5 | 20020225 | AU 2001-78738 | 20010815 |
| PRIORITY APPLN. INFO.: | | | JP 2000-246910 | A 20000816 |
| | | | WO 2001-JP7037 | W 20010815 |

OTHER SOURCE(S): MARPAT 136:177969
 AB Disclosed are medicinal compns. for preventing or treating cancer wherein one or more Peroxisome proliferator-activated receptor .gamma. (PPAR.gamma.) activation agonists and one or more retinoid X receptor (RXR) activation agonists are used simultaneously or successively. A combined administration of 5-[4-(6-methoxy-1-methylbenzimidazol-2-ylmethoxy)benzyl]thiazolidine-2,4-dione hydrochloride (I) 5 and targretin 100 mg/kg to HL-60 cell-bearing mice showed synergistic antitumor effect. Also, tablets were prep'd. from I 0.004, targretin 0.1, lactose 0.244, corn starch 50, and magnesium stearate 0.002 g.
 IT 213252-19-8
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (simultaneous or successive use of PPAR.gamma. agonists and RXR agonists for prevention or treatment of cancer)
 RN 213252-19-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 16 OF 42 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2002:142506 CAPLUS
 DOCUMENT NUMBER: 136:177977
 TITLE: Methods for treating inflammatory diseases using PPAR agonists
 INVENTOR(S): Pershad Singh, Harrihar A.
 PATENT ASSIGNEE(S): USA
 SOURCE: PCT Int. Appl., 42 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

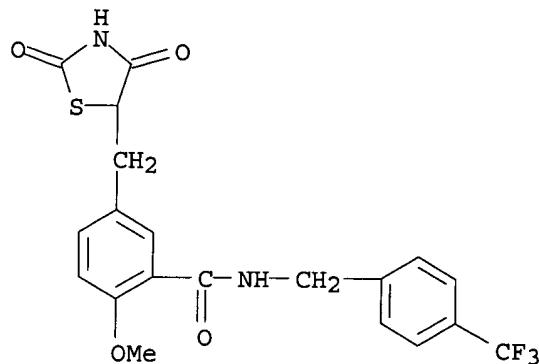
| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2002013812 | A1 | 20020221 | WO 2001-US25668 | 20010816 |
| W: AU, CA, MX, NZ, US
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR | | | | |
| AU 2001088271 | A5 | 20020225 | AU 2001-88271 | 20010816 |
| PRIORITY APPLN. INFO.: | | | US 2000-225907P | P 20000817 |
| | | | US 2000-230509P | P 20000906 |
| | | | WO 2001-US25668 | W 20010816 |

AB The present invention describes methods for the use of PPAR ligands in the treatment of inflammatory, endocrine, dermatological, cardiovascular, immunological, neurological, ophthalmic, neoplastic, pulmonary diseases, and age-related dysregulations. In addition, methods are provided for treating said conditions and diseases comprising the step of administering to a human or an animal in need thereof a therapeutic amount of pharmacological compounds comprising a pharmaceutically acceptable carrier, and a PPAR gamma agonist which cross-activates PPAR alpha or PPAR delta or both, or a PPAR gamma partial agonist, or a PPAR gamma / RXR agonist, effective to reverse, slow, stop, or prevent the pathological inflammatory or degenerative process.

IT 213252-19-8, KRP 297
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (methods for treating inflammatory diseases using PPAR agonists)

RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)

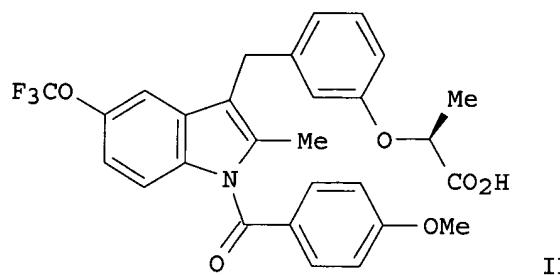
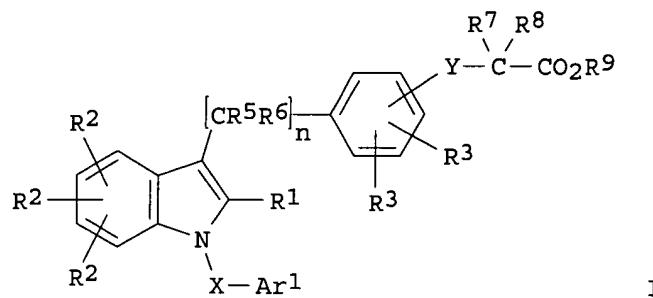


REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

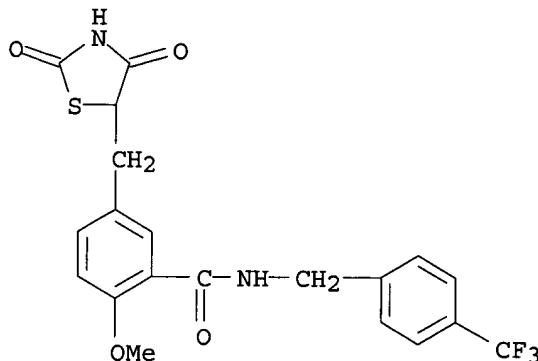
L4 ANSWER 17 OF 42 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2002:90008 CAPLUS
 DOCUMENT NUMBER: 136:151071
 TITLE: Preparation of N-substituted indoles for treating diabetes
 INVENTOR(S): Acton, John J., III; Black, Regina Marie; Jones, Anthony Brian; Wood, Harold Blair
 PATENT ASSIGNEE(S): Merck & Co., Inc., USA
 SOURCE: PCT Int. Appl., 73 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2002008188 | A1 | 20020131 | WO 2001-US22979 | 20010720 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| US 2002042441 | A1 | 20020411 | US 2001-912961 | 20010725 |
| US 6525083 | B2 | 20030225 | | |

PRIORITY APPLN. INFO.: US 2000-220778P P 20000725
 OTHER SOURCE(S): MARPAT 136:151071
 GI



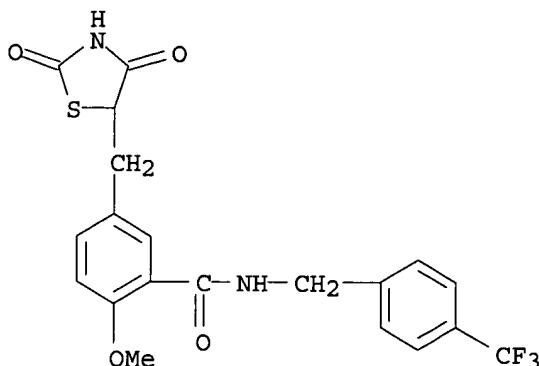
- AB** The title indoles having aryloxyacetic acid substituents [I; R1 = Me, optionally substituted with 1-3 F atoms; R2-R4 = H, halo, alkyl, etc.; R5, R6 = H, F, OH, alkyl; and R5 and R6 groups that are on the same carbon atom optionally may be joined to form a cyclopropyl group; R7, R8 = H, F, alkyl; or CR7R8 may form cycloalkyl; R9 = H, alkyl; Ar1 = (un)substituted Ph, naphthyl, pyridyl, quinolyl; X = CO, SO2, CH2, CHMe, CMe2, CF2, cyclopropylidene; Y = O, S; n = 0-5] which are agonists or partial agonists of PPAR gamma, and are useful in the treatment, control or prevention of non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR mediated diseases, disorders and conditions, were prep'd. E.g., a multi-step synthesis of (2S)-II was given.
- IT** **213252-19-8**, KRP-297
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of N-substituted indoles for treating diabetes)
- RN** 213252-19-8 CAPLUS
- CN** Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

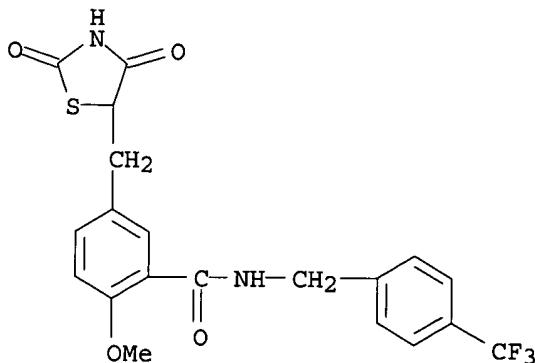
L4 ANSWER 18 OF 42 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2002:56491 CAPLUS
 DOCUMENT NUMBER: 137:73203
 TITLE: Pharmacological analysis of wild-type .alpha., .gamma. and .delta. subtypes of the human peroxisome proliferator-activated receptor
 AUTHOR(S): Wurch, T.; Junquero, D.; Delhon, A.; Pauwels, P. J.
 CORPORATE SOURCE: Department of Cellular and Molecular Biology, Centre de Recherche Pierre Fabre, Castres, 81106, Fr.
 SOURCE: Naunyn-Schmiedeberg's Archives of Pharmacology (2002), 365(2), 133-140
 CODEN: NSAPCC; ISSN: 0028-1298
 PUBLISHER: Springer-Verlag
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Three distinct peroxisome proliferator-activated receptor (PPAR) cDNAs were isolated from human brain RNA. Whereas the PPAR.delta. subtype perfectly matched the amino acid sequences reported in the Genbank database, several differences were found for the PPAR.alpha. (Lys123Met, Ala268Val, Gly296Ala and Val444Ala) and PPAR.gamma.2 (Met8Ile, Pro9Ala, Met186Ile, Pro187Ala and the deletion of a Gln213 residue) subtypes. A pharmacol. anal. was undertaken by co-expressing each PPAR subtype with a reporter plasmid contg. a luciferase gene under the transcriptional control of a synthetic, triplicated PPAR response element in either HepG2 or Cos-7 cells. Whereas fenofibrate unselectively activated the PPAR.alpha. and PPAR.delta. subtypes, the related BM-17.0744 compd. was more potent and selective for PPAR.alpha.. The thiazolidine dione derivs. rosiglitazone and pioglitazone were potent and selective PPAR.gamma.2 agonists. L-165041, reported as a selective and potent PPAR.delta. ligand, displayed in this specified transactivation system, apart from its highly efficacious PPAR.delta. agonist activity, partial and full agonism at, resp., PPAR.alpha. and PPAR.gamma.2 subtypes. In conclusion, transcriptional control of a luciferase gene by wild-type PPAR subtypes provides powerful recombinant assays to evaluate ligand's efficacy at these nuclear receptors.
 IT 213252-19-8, KRP-297
 RL: PAC (Pharmacological activity); BIOL (Biological study)
 (pharmacol. anal. of wild-type .alpha., .gamma. and .delta. subtypes of human peroxisome proliferator-activated receptor)
 RN 213252-19-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-

(trifluoromethyl)phenyl]methyl] - (9CI) (CA INDEX NAME)



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 19 OF 42 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2001:900080 CAPLUS
 DOCUMENT NUMBER: 136:318816
 TITLE: Design, synthesis and evaluation of substituted phenylpropanoic acid derivatives as peroxisome proliferator-activated receptor (PPAR) activators: novel human PPAR. α -selective activators
 AUTHOR(S): Miyachi, Hiroyuki; Nomura, Masahiro; Tanase, Takahiro; Takahashi, Yukie; Ide, Tomohiro; Tsunoda, Masaki; Murakami, Koji; Awano, Katsuya
 CORPORATE SOURCE: Kyorin Pharmaceutical Co., Ltd., Discovery Research Laboratories, Tochigi, Shimotsuga-gun, Nogi-machi, 329-0114, Japan
 SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), Volume Date 2002, 12(1), 77-80
 CODEN: BMCLE8; ISSN: 0960-894X
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB A series of substituted phenylpropanoic acid derivs. was prep'd. as part of a search for subtype-selective human peroxisome proliferator-activated receptor (PPAR) activators. Structure-activity relationship studies indicated that the substituent at the α -position of the carboxyl group plays a key role in detg. the potency and the selectivity for PPAR transactivation.
 IT 213252-19-8, KRP 297
 RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (design, synthesis and evaluation of substituted phenylpropanoic acid derivs. as PPAR activators)
 RN 213252-19-8 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl] - (9CI) (CA INDEX NAME)



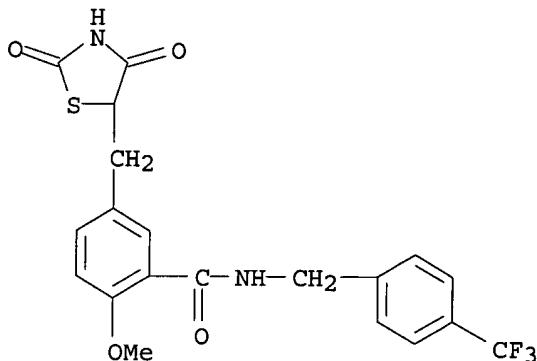
REFERENCE COUNT: 19 THERE ARE 19 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 20 OF 42 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2001:798208 CAPLUS
 DOCUMENT NUMBER: 135:344474
 TITLE: Preparation of novel stable crystal of thiazolidinedione derivative
 INVENTOR(S): Oonoda, Michiro; Orita, Kazuo
 PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 17 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|----------|--|------------|
| WO 2001081327 | A1 | 20011101 | WO 2001-JP3450 | 20010423 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2001048828 | A5 | 20011107 | AU 2001-48828 | 20010423 |
| BR 2001010258 | A | 20030107 | BR 2001-10258 | 20010423 |
| EP 1277745 | A1 | 20030122 | EP 2001-921997 | 20010423 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| NO 2002005069 | A | 20021022 | NO 2002-5069 | 20021022 |
| PRIORITY APPLN. INFO.: | | | JP 2000-124006 A | 20000425 |
| | | | WO 2001-JP3450 | W 20010423 |
| AB | Claimed is a crystal of 5-[(2,4-dioxothiazolidin-5-yl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]benzamide (KRP-297) having diffraction angles (2.theta.) at least 9.7.degree., 15.0.degree., and 22.5.degree. in X-ray powder diffractometry. The novel crystal of KRP-297 (a known antidiabetic agent) is prep'd. through recrystn. from an alc. solvent. | | | |
| IT | 353275-24-8P | | RL: IMF (Industrial manufacture); RCT (Reactant); SPN (Synthetic | |

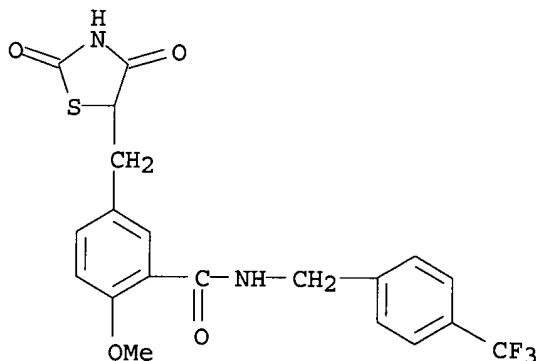
10049937

preparation); PREP (Preparation); RACT (Reactant or reagent)
(prepn. of novel stable crystal of thiazolidinedione deriv.)
RN 353275-24-8 CAPLUS
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]-, monosodium salt (9CI) (CA INDEX NAME)



● Na

IT 213252-19-8P, KRP-297
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); THU
(Therapeutic use); BIOL (Biological study); PREP (Preparation); USES
(Uses)
(prepn. of novel stable crystal of thiazolidinedione deriv.)
RN 213252-19-8 CAPLUS
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]-, (9CI) (CA INDEX NAME)

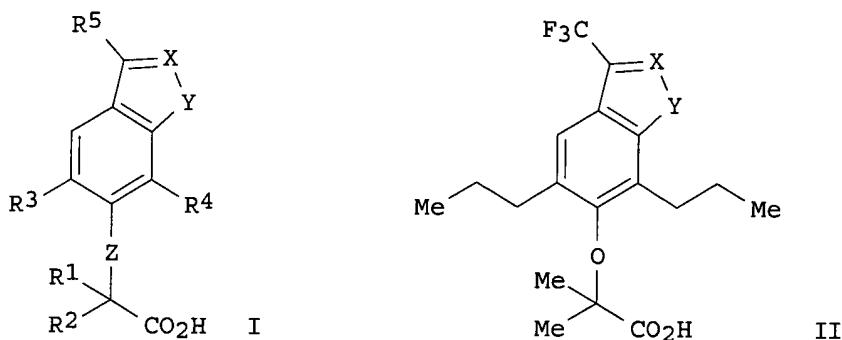


REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 21 OF 42 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2001:617987 CAPLUS
DOCUMENT NUMBER: 135:180757
TITLE: Preparation of 1,2-benzoxazolyloxyacetic acids and analogs as PPAR agonists for treatment of diabetes and

lipid disorders
 INVENTOR(S) : Liu, Kun; Xu, Libo; Jones, A. Brian
 PATENT ASSIGNEE(S) : Merck + Co. Inc., USA
 SOURCE: PCT Int. Appl., 54 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|-------------------|-----------------|------------|
| WO 2001060807 | A1 | 20010823 | WO 2001-US4636 | 20010214 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,
HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU,
LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD,
SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU,
ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1259494 | A1 | 20021127 | EP 2001-910624 | 20010214 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| PRIORITY APPLN. INFO.: | | | US 2000-183593P | P 20000218 |
| | | | WO 2001-US4636 | W 20010214 |
| OTHER SOURCE(S) : | | MARPAT 135:180757 | | |
| GI | | | | |



AB The title compds. (I) [wherein R1 and R2 = independently H, F, (halo)alkyl, (halo)alkenyl, (halo)alkynyl; or R1 and R2 may form a cycloalkyl group; R3 and R4 = independently (fluoro)alkyl, (fluoro)alkenyl, (fluoro)alkynyl, or Cl; X = N or CR; Y = O, S, nor NR; Z = O or S; R = independently H or optionally fluoroo- or alkoxy-substituted (cyclo)alkyl(oxy), alkenyl(oxy), or alkynyl(oxy); R5 = H or (un)substituted alkyl, alkenyl, alkynyl, (hetero)aryl(oxy), heterocyclyl(oxy), etc.; and pharmaceutically acceptable salts and prodrugs thereof] were prep'd. For example, 2,4-dihydroxy-3,5-dipropyl-1',1',1'-trifluoroacetophenone oxime was acetylated and then treated with pyridine and TEA to give 5,7-dipropyl-6-hydroxy-3-trifluoromethyl-1,2-

benzisoxazole. Etherification with Me .alpha.-bromoisobutyrate in the presence of Cs₂CO₃ in DMF, followed by sapon., afforded the 1,2-benzoxazolyloxyacetic acid (II). I are potent agonists of peroxisome proliferator activated receptor (PPAR) .alpha. and/or .gamma. and are useful in the treatment, control, or prevention of non-insulin dependent diabetes mellitus (NIDDM), hyperglycemia, dyslipidemia, hyperlipidemia, hypercholesterolemia, hypertriglyceridemia, atherosclerosis, obesity, vascular restenosis, inflammation, and other PPAR.alpha. and/or .gamma. mediated diseases, disorders, and conditions (no data).

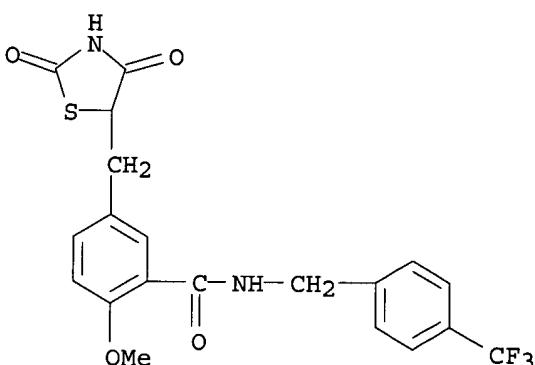
IT 213252-19-8, KRP-297

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(coadministration with; prepn. of benzisoxazolyloxyacetic acid PPAR agonists via cyclization of dihydroxyacetophenone oximes for treatment of diabetes and lipid disorders)

RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 22 OF 42 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:617810 CAPLUS

DOCUMENT NUMBER: 135:175429

TITLE: Modulation of bone formation with peroxisome proliferator-activated receptor activators and ligands

INVENTOR(S): Scutt, Andrew; Still, Karen

PATENT ASSIGNEE(S): University of Sheffield, UK

SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|---|----------|-----------------|----------|
| WO 2001060355 | A1 | 20010823 | WO 2001-GB626 | 20010215 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, | | | |

LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,
 SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN,
 YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,
 BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

EP 1259233 A1 20021127 EP 2001-904207 20010215

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR

NO 2002003837 A 20021014 NO 2002-3837 20020814

PRIORITY APPN. INFO.: GB 2000-3310 A 20000215
 WO 2001-GB626 W 20010215

AB The use of an activator or ligand of a peroxisome proliferator-activated receptor, other than PPAR. γ , or pharmaceutically acceptable deriv. of said activator or ligand, in the manuf. of a medicament for the treatment or prophylaxis of bone disease allows, for the first time, bone anabolism to enhance the deposition of bone in conditions which would benefit from increased bone deposition. The reverse, where there is inhibition and/or retardation of bone deposition is also facilitated.

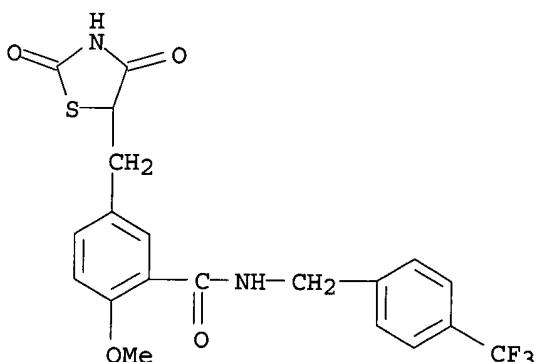
IT 213252-19-8, KRP-297

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(modulation of bone formation with peroxisome proliferator-activated receptor activators and ligands)

RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



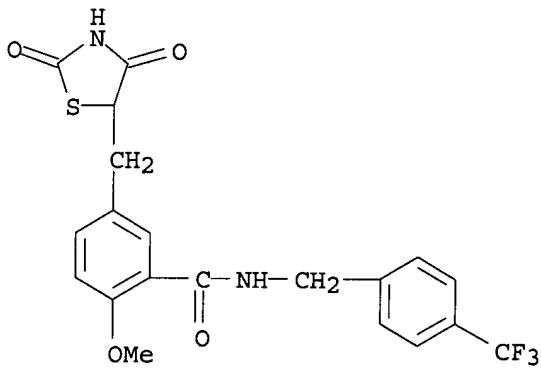
REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 23 OF 42 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2001:581862 CAPLUS
 DOCUMENT NUMBER: 135:152800
 TITLE: Alkali metal salt of thiazolidine-2,4-dione derivative and purification of KRP-297
 INVENTOR(S): Ohnoda, Michiro; Orita, Kazuo; Yoshida, Noriyuki
 PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: PCT Int. Appl., 17 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|---|----------|-----------------|------------|
| WO 2001057007 | A1 | 20010809 | WO 2001-JP598 | 20010130 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| AU 2001028854 | A5 | 20010814 | AU 2001-28854 | 20010130 |
| EP 1253145 | A1 | 20021030 | EP 2001-948982 | 20010130 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | |
| US 2003013749 | A1 | 20030116 | US 2002-181432 | 20020725 |
| PRIORITY APPLN. INFO.: | | | JP 2000-23610 | A 20000201 |
| | | | WO 2001-JP598 | W 20010130 |
| AB | This document discloses a method of industrially advantageously purifying 5-[(2,4-dioxothiazolidin-5-yl)methyl]-2-methoxy-N-[4-(trifluoromethyl)phenylmethyl]benzamide (KRP-297), a known antidiabetic agent. The method comprises the steps of: forming an alkali metal salt of KRP-297 and a hydrate thereof in a reaction for producing KRP-297; isolating and purifying them; and then liberating the KRP-297 from the salt. Also provided are an alkali metal salt of KRP-297 and a hydrate of the salt. | | | |
| IT | 213252-19-8P, KRP 297
RL: PUR (Purification or recovery); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(purifn. of antidiabetic KRP-297) | | | |
| RN | 213252-19-8 CAPLUS | | | |
| CN | Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[4-(trifluoromethyl)phenylmethyl]- (9CI) (CA INDEX NAME) | | | |



IT 353275-24-8P 353275-26-0P 353275-27-1P

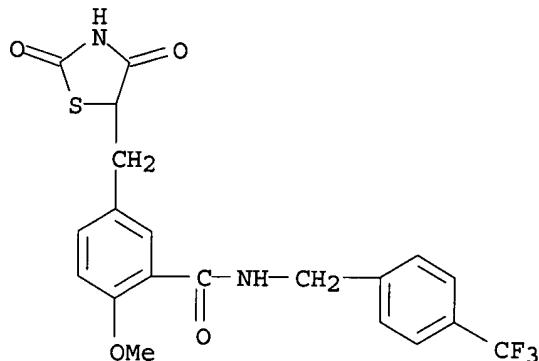
353275-28-2P

RL: SPN (Synthetic preparation); PREP (Preparation)
(purifn. of antidiabetic KRP-297)

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RN 353275-24-8 CAPLUS

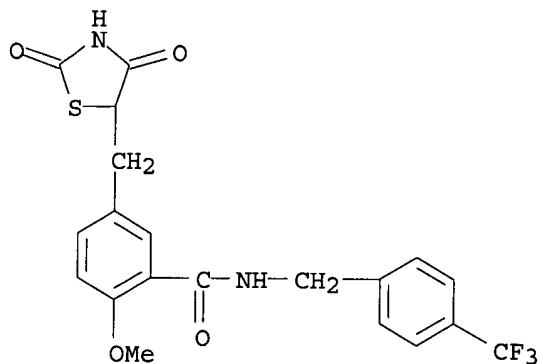
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]-, monosodium salt (9CI) (CA INDEX NAME)



● Na

RN 353275-26-0 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]-, monosodium salt, monohydrate (9CI) (CA INDEX NAME)

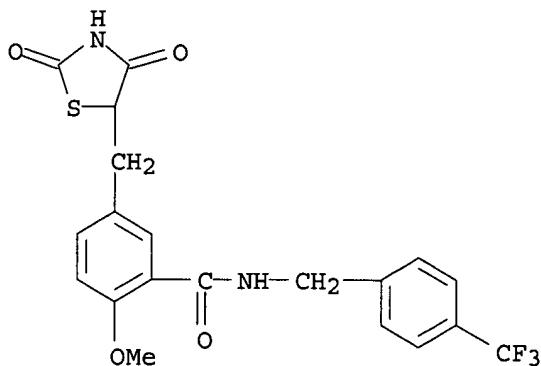


● Na

● H₂O

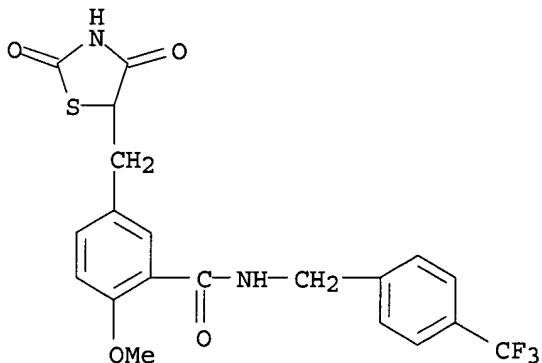
RN 353275-27-1 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]-, monopotassium salt (9CI) (CA INDEX NAME)



● K

RN 353275-28-2 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[4-(trifluoromethyl)phenyl]methyl-, monopotassium salt, monohydrate (9CI)
(CA INDEX NAME)

● K

● H₂O

REFERENCE COUNT: 33 THERE ARE 33 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 24 OF 42 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:564869 CAPLUS

DOCUMENT NUMBER: 135:132451

TITLE: Novel remedies with the use of .beta.3 agonists

INVENTOR(S): Ogawa, Kohei; Umeno, Hiroshi

PATENT ASSIGNEE(S): Asahi Kasei K. K., Japan

SOURCE: PCT Int. Appl., 49 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2001054728 | A1 | 20010802 | WO 2001-JP553 | 20010126 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2001027103 | A5 | 20010807 | AU 2001-27103 | 20010126 |
| EP 1258253 | A1 | 20021120 | EP 2001-901552 | 20010126 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| US 2003018061 | A1 | 20030123 | US 2002-182375 | 20020729 |

PRIORITY APPLN. INFO.: JP 2000-20733 A 20000128
 WO 2001-JP553 W 20010126

AB Remedies contg. at least one member selected from the group consisting of cholinolytics, monoamine reuptake inhibitors, lipase inhibitors, selective serotonin reuptake inhibitors, insulin, insulin secretion promoters, biguanide, .alpha.-glucosidase inhibitors, insulin resistance improving agents, HMC-CoA reductase inhibitors, anion exchange resins, clofibrate-base drugs and nicotinic acid-base drugs and a compd. having a .beta.3-agonistic activity. The .beta.3 agonist has an activity of inhibiting urination disorder. When used together with a remedy for urination disorder such as propiverine, oxybutynin hydrochloride or tolterodine, it exerts an enhanced anti-urination disorder effect. When used together with an antiobesity agent such as sibutramine or orlistat, it exerts an enhanced antiobesity effect. When used together with an antidiabetic agent such as insulin, glibenclamide, acarbose or rosiglitazone, it exerts an enhanced antidiabetic effect. When used together with an antilipemic drug such as bezafibrate or pravastatin, it exerts an enhanced antilipemic effect.

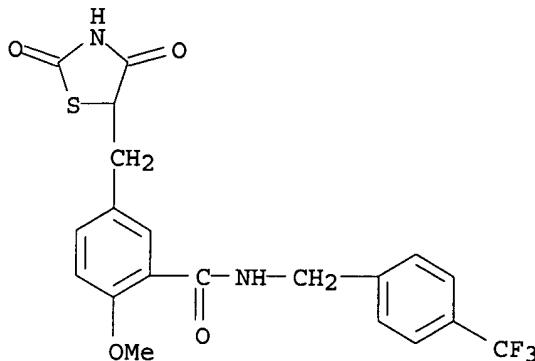
IT 213252-19-8, KRP 297

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(novel remedies with the use of .beta.3 agonists as antidiabetics and antilipidemics and for treatment of urination disorder)

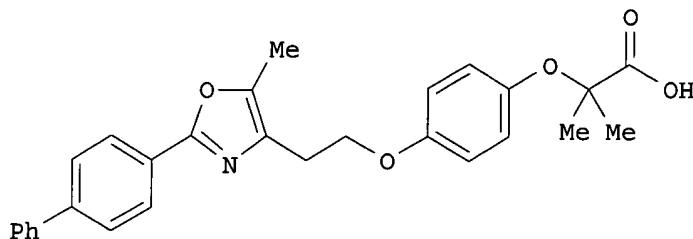
RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 43 THERE ARE 43 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 25 OF 42 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2001:367156 CAPLUS
 DOCUMENT NUMBER: 135:131731
 TITLE: Design and Synthesis of 2-Methyl-2-{4-[2-(5-methyl-2-aryloxazol-4-yl)ethoxy]phenoxy}propionic Acids: A New Class of Dual PPAR. α ./.math>. Agonists
 AUTHOR(S): Brooks, Dawn A.; Etgen, Garret J.; Rito, Christopher J.; Shuker, Anthony J.; Dominianni, Samuel J.; Warshawsky, Alan M.; Ardecky, Robert; Paterniti, James R.; Tyhonas, John; Karanewsky, Donald S.; Kauffman, Raymond F.; Broderick, Carol L.; Oldham, Brian A.; Montrose-Rafizadeh, Chahzrad; Winneroski, Leonard L.; Faul, Margaret M.; McCarthy, James R.
 CORPORATE SOURCE: Lilly Research Laboratories A Division of Eli Lilly Company Lilly Corporate Center, Indianapolis, IN, 46285, USA
 SOURCE: Journal of Medicinal Chemistry (2001), 44(13), 2061-2064
 CODEN: JMCMAR; ISSN: 0022-2623
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 OTHER SOURCE(S): CASREACT 135:131731
 GI



I

AB Propionic acid deriv. I, which was designed and synthesized based on putative pharmacophores of known PPAR. γ - and PPAR. α -selective compds., exhibits potent dual PPAR. α ./.math>. agonist activity as

demonstrated by in vitro binding and dose overlap in the newly introduced EOB mouse model for glucose lowering and lipid/cholesterol homeostasis.

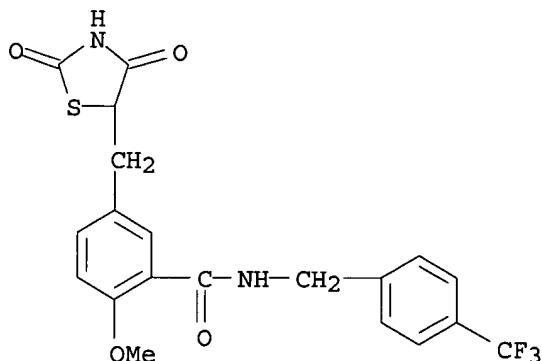
IT 213252-19-8, KRP-297

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(design and synthesis of 2-methyl-2-{4-[2-(5-methyl-2-aryloxazol-4-yl)ethoxy]phenoxy}propionic acids: a new class of dual PPAR. α ./ γ . agonists)

RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 26 OF 42 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:359797 CAPLUS

DOCUMENT NUMBER: 134:344620

TITLE: Solid oral composition containing KRP-297

INVENTOR(S): Ohyama, Toshinori; Imamizu, Masaru

PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 11 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2001034148 | A1 | 20010517 | WO 2000-JP7905 | 20001110 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2001013046 | A5 | 20010606 | AU 2001-13046 | 20001110 |
| EP 1243266 | A1 | 20020925 | EP 2000-974882 | 20001110 |

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL, TR
 PRIORITY APPLN. INFO.: JP 1999-320586 A 19991111
 WO 2000-JP7905 W 20001110

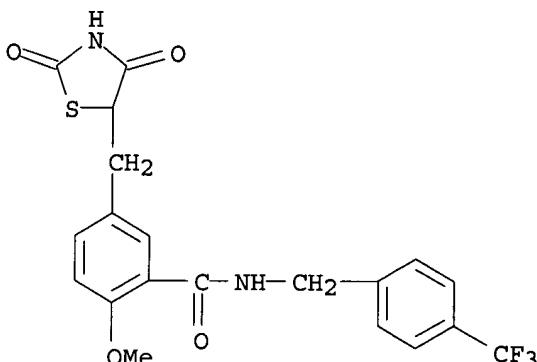
AB Disclosed are solid compns. for oral use for facilitating the administration in a small dose of KRP-297, which is a ligand common to peroxisome proliferator-activated receptors PPAR.alpha. and PPAR.gamma. (i.e., nuclear receptors) and has an effect of ameliorating insulin resistance, which contain the drug ingredient in a uniform content and can be easily and quant. taken. By prep. solid compns. for oral use composed of a trace amt. of the drug ingredient together with pharmaceutical carriers, it is possible to provide tablets which contain the drug component in a uniform content and can be easily and quant. taken. A film-coated tablet was prep'd. from KRP-297 0.25, lactose 78.55, cryst. cellulose 26.2, low-substituted hydroxypropyl cellulose 12, polyvinyl alc. 2.4, magnesium stearate 0.6, hydroxypropyl Me cellulose, and carnauba wax 0.001 mg.

IT 213252-19-8, KRP-297

RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (solid oral compns. contg. uniform contents of KRP-297)

RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

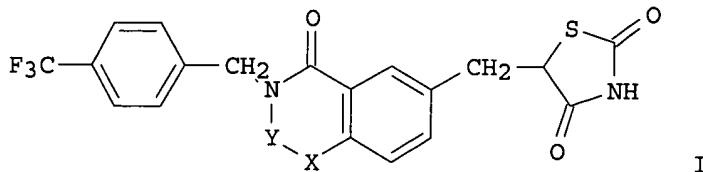


REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 27 OF 42 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2001:347100 CAPLUS
 DOCUMENT NUMBER: 134:353303
 TITLE: preparation of thiazolidinyl-containing bicyclic heterocycles as humane peroxisome proliferator-activated receptor .gamma. agonists
 INVENTOR(S): Nomura, Masahiro; Murakami, Koji; Kakuta, Masaki
 PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
 CODEN: JKXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

 JP 2001131173 A2 20010515 JP 2000-242708 20000810
 PRIORITY APPLN. INFO.: JP 1999-235531 A 19990823
 OTHER SOURCE(S) : MARPAT 134:353303
 GI



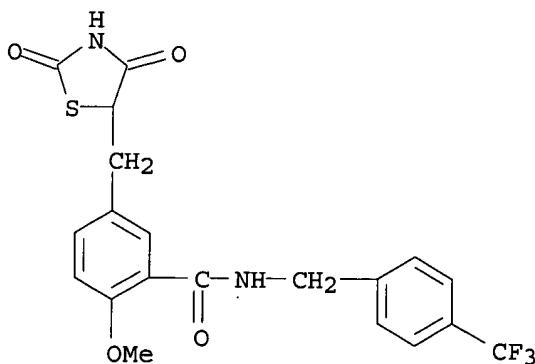
AB Title compds. I ($\text{YX} = \text{CO}_2$, CH_2O , $\text{CH}:\text{CH}$), their pharmaceutically acceptable salts, or hydrates, useful as for treatment of Type II diabetes and hyperlipemia, are prep'd. 2-Hydroxy-5-[(2,4-dioxothiazolidin-5-yl)methyl]-N-[(4-trifluorophenyl)methyl]benzamide was reacted with trioxane in the presence of AcOH in CH_2Cl_2 at room temp. for 2 day to give 42% 6-[(2,4-dioxothiazolidin-5-yl)methyl]-3-[(4-trifluorophenyl)methyl]-1,3-benzoxazin-4-one showing good transcription activity of proliferator-activated receptor γ . in vitro.

IT 213252-19-8

RL: RCT (Reactant); RACT (Reactant or reagent)
 (prepn. of bicyclic heterocycles as humane peroxisome proliferator-activated receptor γ . agonists)

RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)

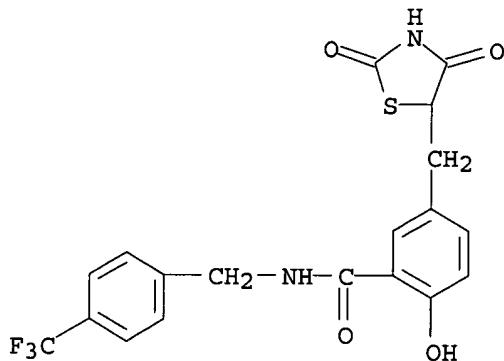


IT 223508-81-4P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
 (prepn. of bicyclic heterocycles as humane peroxisome proliferator-activated receptor γ . agonists)

RN 223508-81-4 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-hydroxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 28 OF 42 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2001:338335 CAPLUS
 DOCUMENT NUMBER: 134:344604
 TITLE: Antidiabetic formulation containing metformin and sulfonylurea
 INVENTOR(S): Piper, Beth Anne
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
 SOURCE: PCT Int. Appl., 76 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2001032158 | A2 | 20010510 | WO 2000-US28467 | 20001013 |
| WO 2001032158 | A3 | 20020829 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| US 2002177602 | A1 | 20021128 | US 1999-432465 | 19991103 |
| EP 1253944 | A2 | 20021106 | EP 2000-970913 | 20001013 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | |
| NO 2002002086 | A | 20020624 | NO 2002-2086 | 20020502 |
| PRIORITY APPLN. INFO.: | | | US 1999-432465 | A 19991103 |
| | | | WO 2000-US28467 | W 20001013 |

AB A low dose antidiabetic formulation adapted for treating e.g., Type II diabetes contains a combination of metformin (at <800 mg/day) and at least 1 other antidiabetic agent such as a sulfonylurea. This combination provides at least about substantially equiv. efficacy in treating diabetes as do antidiabetic formulations contg. metformin employed in dosages prescribed in generally accepted medical practice for first line therapy in treating diabetes, but with substantially reduced side effects, such as hypoglycemia and/or gastrointestinal distress. A method for treating diabetes in drug naive human patients is also provided employing the above

formulation to reduce insulin resistance and/or post-prandial glucose excursion and/or Hb 1Ac, and/or increase post-prandial insulin, thereby treating the diabetes. Thus, tablets contained metformin-HCl 250.0, glyburide 1.25, croscarmellose sodium 7.00, Povidone 10.00, microcryst. cellulose 28.25, Mg stearate 2.25, and HPMC film-coating 6 mg. The effectiveness of this combination drug in producing hypoglycemia was demonstrated clin.

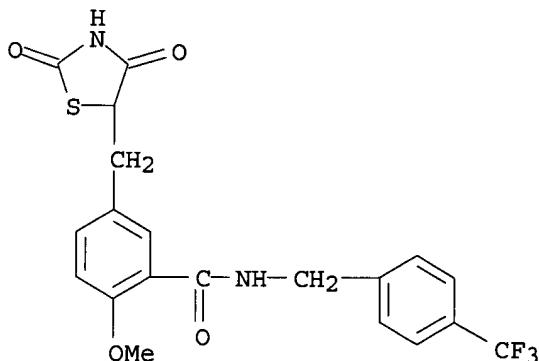
IT 213252-19-8, KRP-297

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(antidiabetic formulation contg. metformin and sulfonylurea)

RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 29 OF 42 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2001:283949 CAPLUS
 DOCUMENT NUMBER: 134:311218
 TITLE: Synthesis and use of heterocyclic sodium/proton exchange inhibitors
 INVENTOR(S): Ahmad, Saleem; Wu, Shung C.; O'Neil, Steven V.; Ngu, Khehyong; Atwal, Karnail S.
 PATENT ASSIGNEE(S): Bristol-Myers Squibb Company, USA
 SOURCE: PCT Int. Appl., 221 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2001027107 | A2 | 20010419 | WO 2000-US27461 | 20001002 |
| WO 2001027107 | A3 | 20020124 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, | | | |

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

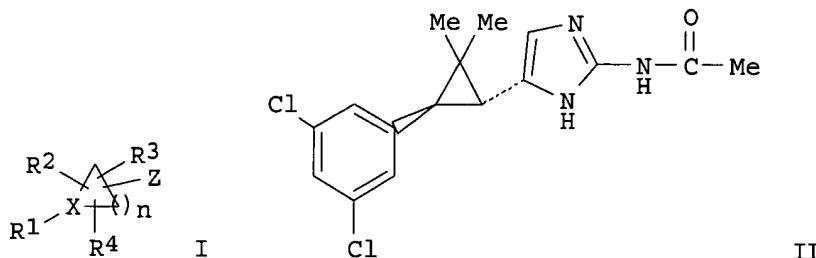
EP 1224183 A2 20020724 EP 2000-968723 20001002

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL

NO 2002001717 A 20020610 NO 2002-1717 20020411

PRIORITY APPLN. INFO.: US 1999-158755P P 19991012
WO 2000-US27461 W 20001002

OTHER SOURCE(S) : MARPAT 134:311218



AB Compds. of formula I [wherein; n is 1-5; X is N or CR₅, where R₅ is H, halo, alkenyl, alkynyl, alkoxy, alkyl, aryl or heteroaryl; Z is a heteroaryl group; R₁ is H, alk(en)(yn)yl, alk(enyl)(ynyl)oxy, (aryl or alkyl)3Si, cycloalk(en)yl, (aryl)amino, aryl(alkyl), cycloheteroaryl, etc.; R₂, R₃ and R₄ are any of the groups set out for R₁ and optionally substituted with 1 to 5 substituents which may be the same or different and when X is N, R₁ is preferably aryl or heteroaryl] are claimed. Several hundred examples are disclosed. Synthesis of II proceeds via cyclopropanation of the cinnamate derived from the olefination between 3,5-dichlorobenzaldehyde and t-butyl diethylphosphonoacetate. The intermediate tert-Bu ester is converted to the corresponding .alpha.-chloroketone and reacted with acetyl guanidine to provide II in a total of 5 steps. Compds. I are said to be sodium/proton exchange inhibitors (NHE). Pharmaceutical combinations are claimed using I and certain antihypertensive agents, .beta.-adrenergic agonists, hypolipidemic agents, antidiabetic agents, antiobesity agents, etc. Compds. I are useful as antianginal and cardioprotective agents and provide a method for preventing or treating angina pectoris, cardiac dysfunction, myocardial necrosis, and arrhythmia.

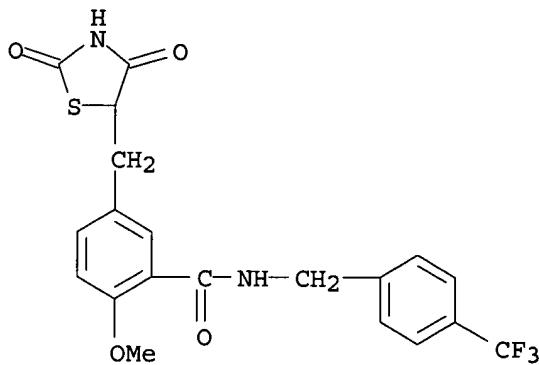
IT 213252-19-8, KRP297

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmaceuticals also contg.; synthesis and use of heterocyclic sodium/proton exchange inhibitors)

RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]-(9CI) (CA INDEX NAME)



L4 ANSWER 30 OF 42 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:152661 CAPLUS

DOCUMENT NUMBER: 134:193428

TITLE: Preparation of substituted benzylthiazolidine-2,4-dione derivatives as agonists of human peroxisome proliferator-activated receptor

INVENTOR(S): Nomura, Masahiro; Murakami, Koji; Tsunoda, Masaki; Takahashi, Yukie

PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 19 pp.

CODEN: PIXXD2

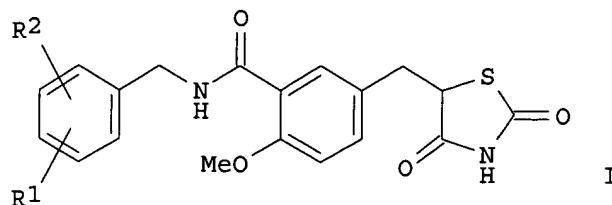
DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|--------|------------|-----------------|------------|
| WO 2001014352 | A1 | 20010301 | WO 2000-JP5522 | 20000818 |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1207158 | A1 | 20020522 | EP 2000-953478 | 20000818 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL | | | | |
| PRIORITY APPLN. INFO.: | | | JP 1999-235530 | A 19990823 |
| | | | WO 2000-JP5522 | W 20000818 |
| OTHER SOURCE(S): | MARPAT | 134:193428 | | |
| GI | | | | |



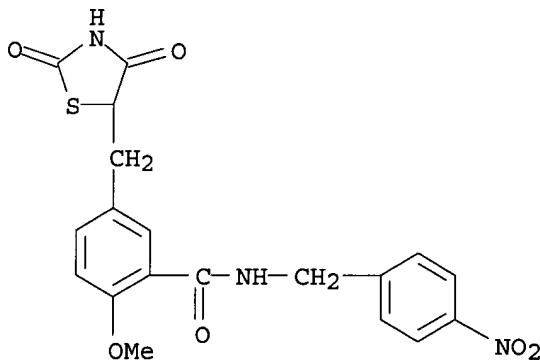
AB The title compds. (I), pharmaceutically acceptable salts thereof and hydrates of the same (wherein R1 represents chloro, bromo, nitro, trifluoromethoxy, ethoxy, propoxy or isopropoxy; and R2 represents hydrogen or chloro) are prep'd. These compds. are capable of, as a ligand of human peroxisome proliferator-activated receptor (PPAR), enhancing the transcriptional activity of the receptor and showing effects of lowering blood sugar level and lowering lipid level; and a process for producing the same. Thus, 5-[(2,4-dioxothiazolidin-5-yl)methyl]-2-methoxybenzoic acid, Et₃N, and CH₂Cl₂ were mixed, treated with Et chlorocarbonate and stirred under ice-cooling for 10 min, treated with 4-nitrobenzylamine, and then stirred at room temp. for 2 h to give 75% N-[(4-nitrophenyl)methyl]-5-[(2,4-dioxothiazolidin-5-yl)methyl]-2-methoxybenzamide (II). II and I (R1 = 4-n-Pro, R2 = H) enhanced the transcriptional activity of human PPAR. α . in CHO cells with EC₅₀ of 0.53 and 0.11 .mu.M, resp.

IT 326926-46-9P 326926-47-0P 326926-48-1P
 326926-49-2P 326926-50-5P 326926-51-6P
 326926-52-7P 326926-53-8P 326926-54-9P,
 N-[(3,4-Dichlorophenyl)methyl]-5-[(2,4-dioxothiazolidin-5-yl)methyl]-2-
 methoxybenzamide
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use);
 BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of substituted benzylthiazolidinedione derivs. as agonists of
 human peroxisome proliferator-activated receptor and blood sugar and
 lipid-lowering agents)

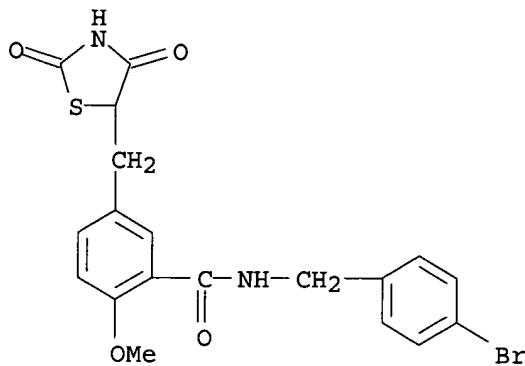
RN 326926-46-9 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-nitrophenyl)methyl]- (9CI) (CA INDEX NAME)

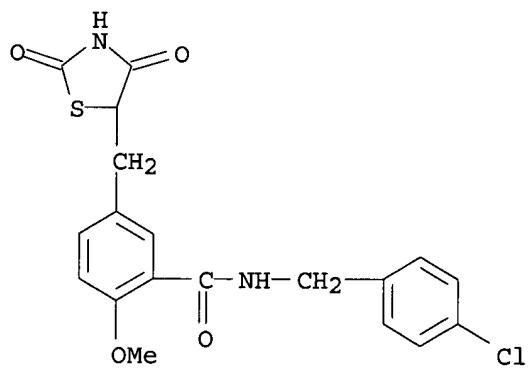


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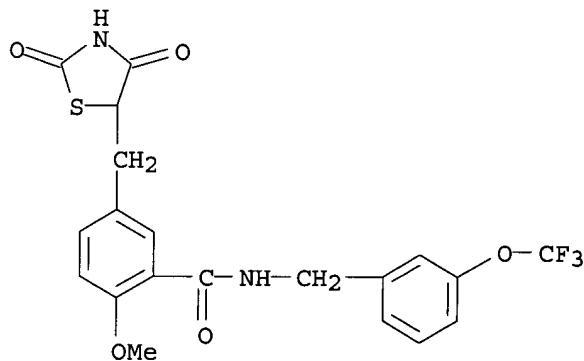
CN Benzamide, N-[(4-bromophenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)



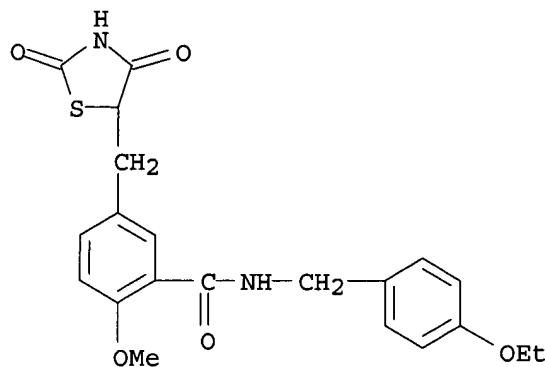
RN 326926-48-1 CAPLUS
 CN Benzamide, N-[(4-chlorophenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)



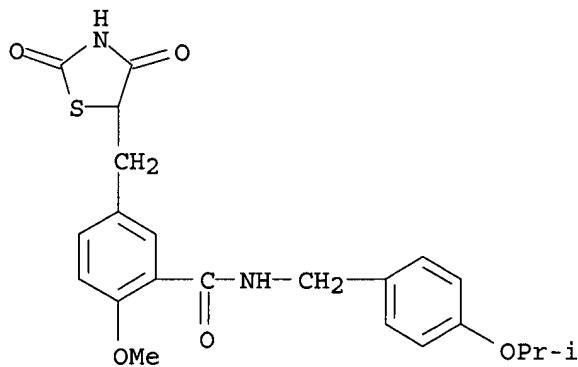
RN 326926-49-2 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(3-trifluoromethoxy)phenyl]methyl- (9CI) (CA INDEX NAME)



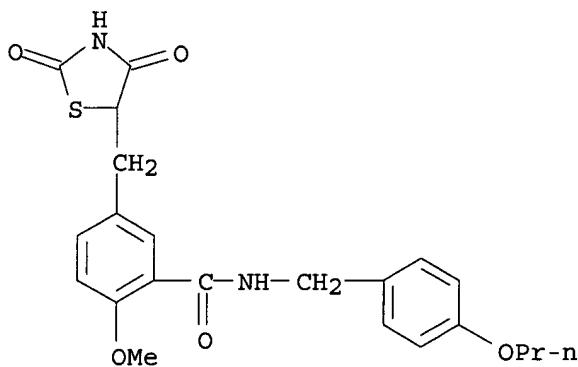
RN 326926-50-5 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-N-[(4-ethoxyphenyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)



RN 326926-51-6 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[4-(1-methylethoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)

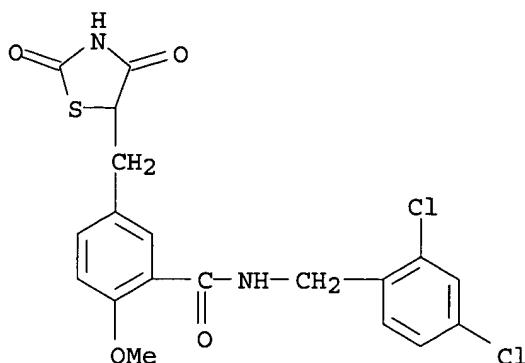


RN 326926-52-7 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-propoxypyhenyl)methyl]- (9CI) (CA INDEX NAME)



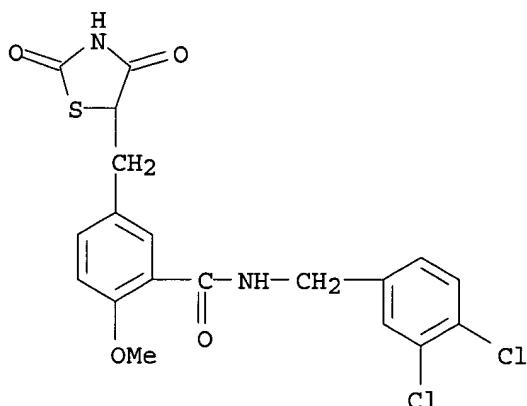
RN 326926-53-8 CAPLUS
 CN Benzamide, N-[(2,4-dichlorophenyl)methyl]-5-[(2,4-dioxo-5-

thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)



RN 326926-54-9 CAPLUS

CN Benzamide, N-[(3,4-dichlorophenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 17 THERE ARE 17 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 31 OF 42 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:152660 CAPLUS

DOCUMENT NUMBER: 134:193427

TITLE: Preparation of substituted benzylthiazolidine-2,4-dione derivatives as agonists of human peroxisome proliferator-activated receptor

INVENTOR(S): Miyachi, Hiroyuki; Nomura, Masahiro; Tanase, Takahiro; Murakami, Koji; Tsunoda, Masaki

PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan

SOURCE: PCT Int. Appl., 20 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

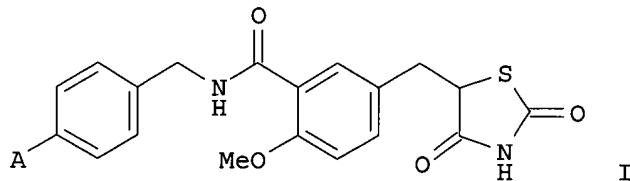
PATENT NO.

KIND DATE

APPLICATION NO. DATE

 WO 2001014351 A1 20010301 WO 2000-JP5521 20000818
 W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU,
 CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL,
 IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD,
 MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK,
 SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY,
 KG, KZ, MD, RU, TJ, TM
 RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
 DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
 CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 EP 1207157 A1 20020522 EP 2000-953477 20000818
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO, MK, CY, AL
 PRIORITY APPLN. INFO.: JP 1999-235529 A 19990823
 JP 2000-242707 A 20000810
 WO 2000-JP5521 W 20000818

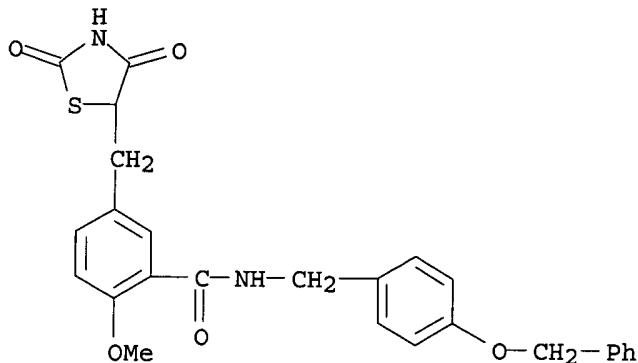
OTHER SOURCE(S): MARPAT 134:193427
 GI



- AB The title compds. represented by general formula (I; wherein A represents optionally substituted Ph, optionally substituted phenoxy or optionally substituted benzyloxy), pharmaceutically acceptable salts thereof and hydrates of the same are prep'd. These compds. are capable of, as a ligand of human peroxisome proliferator-activated receptor (PPAR), enhancing the transcriptional activity of the receptor and showing effects of lowering blood sugar level and lowering lipid level. Thus, 5-[(2,4-dioxothiazolidin-5-yl)methyl]-2-methoxybenzoic acid, Et₃N, and CH₂Cl₂ were mixed, treated with Et chlorocarbonate under ice-cooling, and stirred for 10 min under ice-cooling, followed by adding a soln. of 4-benzyloxybenzylamine in CH₂Cl₂, and the resulting mixt. was stirred at room temp. for 2 h to give 77% N-[(4-benzyloxyphenyl)methyl]-5-[(2,4-dioxothiazolidin-5-yl)methyl]-2-methoxybenzamide (II). II and I (A = PhO) enhanced the transcriptional activity of human PPAR. α . in CHO cells with EC₅₀ of 0.44 and 0.24 .mu.M, resp.
- IT 326925-77-3P 326925-78-4P 326925-79-5P
 326925-80-8P 326925-81-9P 326925-82-0P
 326925-83-1P 326925-84-2P 326925-85-3P
 326925-86-4P 326925-87-5P 326925-88-6P
 326925-89-7P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of substituted benzylthiazolidinedione derivs. as agonists of human peroxisome proliferator-activated receptor and blood sugar and lipid-lowering agents)
- RN 326925-77-3 CAPLUS

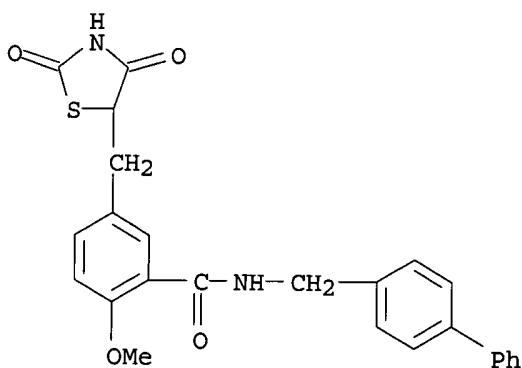
10049937

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(phenylmethoxy)phenyl)methyl]- (9CI) (CA INDEX NAME)



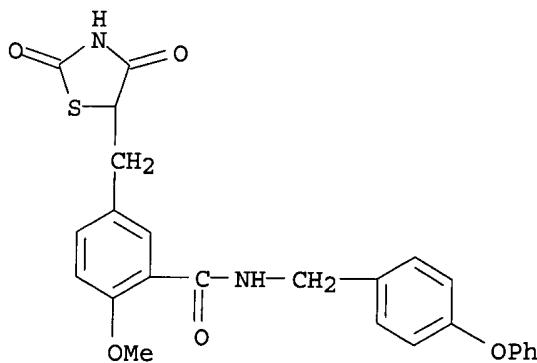
RN 326925-78-4 CAPLUS

CN Benzamide, N-([1,1'-biphenyl]-4-ylmethyl)-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)



RN 326925-79-5 CAPLUS

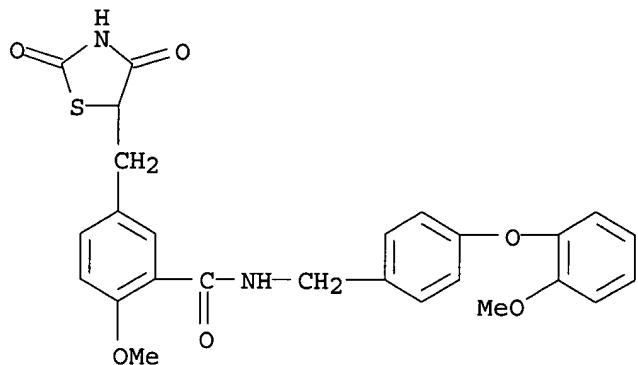
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-phenoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



10049937

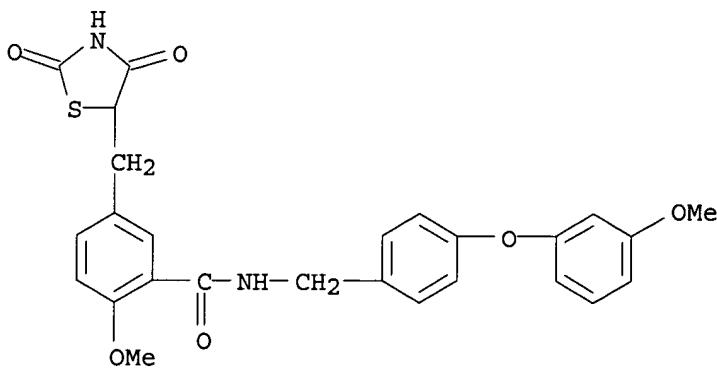
RN 326925-80-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(2-methoxyphenoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)



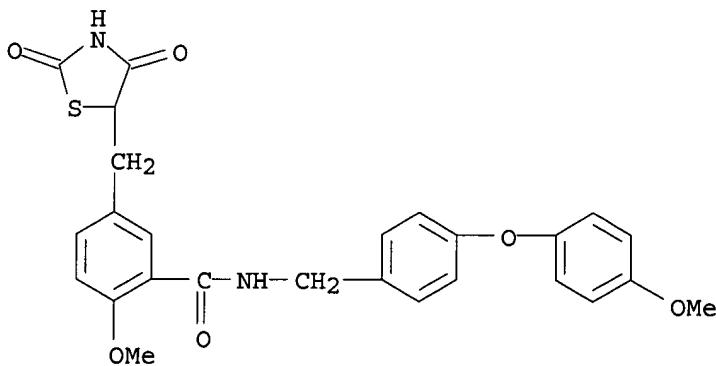
RN 326925-81-9 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(3-methoxyphenoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 326925-82-0 CAPLUS

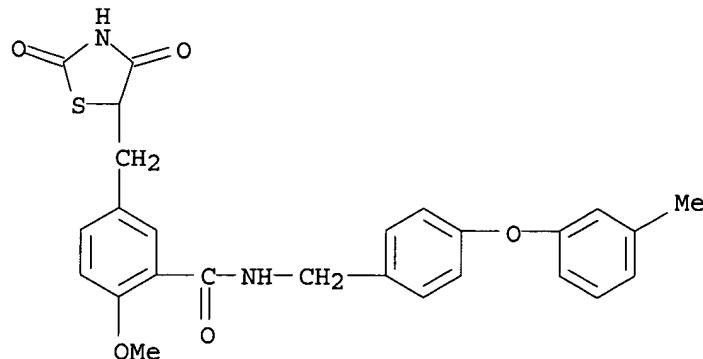
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(4-methoxyphenoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)



10049937

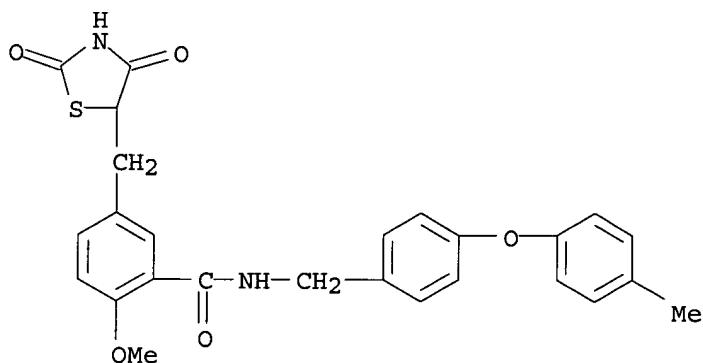
RN 326925-83-1 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(3-methylphenoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)



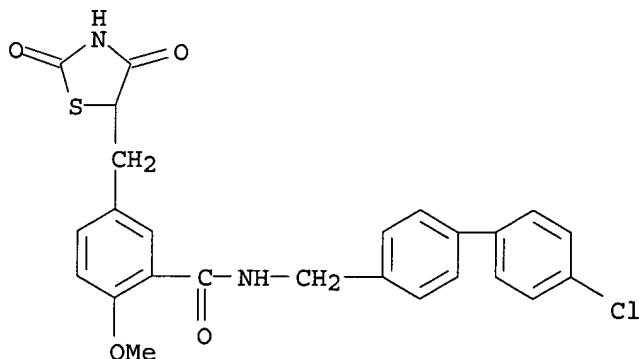
RN 326925-84-2 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(4-methylphenoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 326925-85-3 CAPLUS

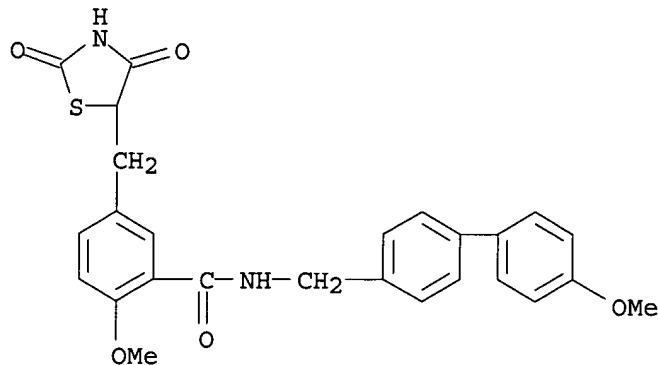
CN Benzamide, N-[(4'-chloro[1,1'-biphenyl]-4-yl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)



10049937

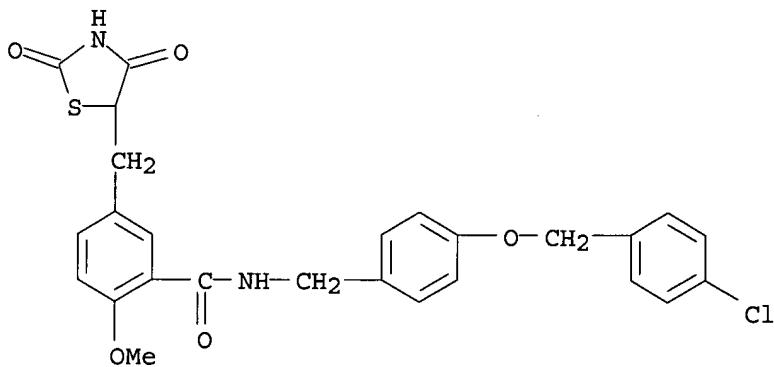
RN 326925-86-4 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4'-methoxy[1,1'-biphenyl]-4-yl)methyl]- (9CI) (CA INDEX NAME)



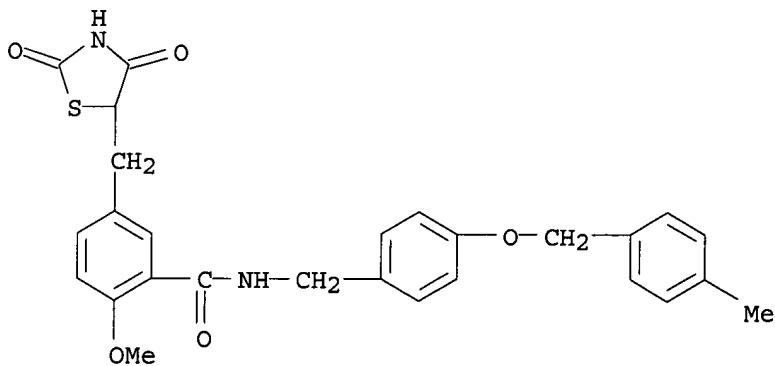
RN 326925-87-5 CAPLUS

CN Benzamide, N-[[4-[(4-chlorophenyl)methoxy]phenyl]methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)

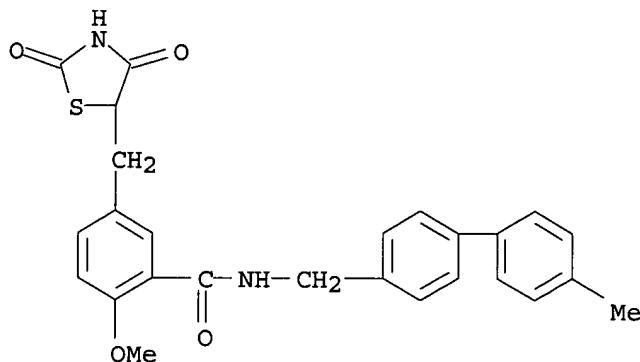


RN 326925-88-6 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-[(4-methylphenyl)methoxy]phenyl]methyl]- (9CI) (CA INDEX NAME)



RN 326925-89-7 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4'-methyl[1,1'-biphenyl]-4-yl)methyl]- (9CI) (CA INDEX NAME)



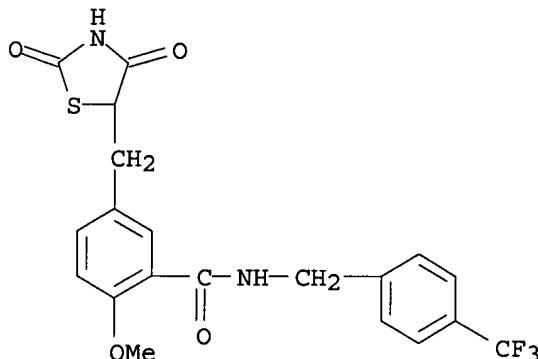
REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 32 OF 42 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 2000:293502 CAPLUS
 DOCUMENT NUMBER: 133:84110
 TITLE: Fenofibrate and Rosiglitazone Lower Serum Triglycerides with Opposing Effects on Body Weight
 AUTHOR(S): Chaput, Evelyne; Saladin, Regis; Silvestre, Martine; Edgar, Alan D.
 CORPORATE SOURCE: Department of Metabolic Diseases, Laboratoire Fournier, Daix, 21121, Fr.
 SOURCE: Biochemical and Biophysical Research Communications (2000), 271(2), 445-450
 CODEN: BBRCA9; ISSN: 0006-291X
 PUBLISHER: Academic Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB Activators of peroxisome proliferator activated receptors (PPARs) are effective drugs to improve the metabolic abnormalities linking hypertriglyceridemia to diabetes, hyperglycemia, insulin-resistance, and atherosclerosis. We compared the pharmacol. profile of a PPAR.alpha. activator, fenofibrate, and a PPAR.gamma. activator, rosiglitazone, on serum parameters, target gene expression, and body wt. gain in (fa/fa) fatty Zucker rats and db/db mice as well as their assocn. in db/db mice. Fenofibrate faithfully modified the expression of PPAR.alpha. responsive genes. Rosiglitazone increased adipose tissue aP2 mRNA in both models while increasing liver acyl CoA oxidase mRNA in db/db mice but not in fatty Zucker rats. Both drugs lowered serum triglycerides yet rosiglitazone markedly increased body wt. gain while fenofibrate decreased body wt. gain in fatty Zucker rats. KRP 297, which has been reported to be a PPAR.alpha. and .gamma. co-activator, also affected serum triglycerides and insulin in fatty Zucker rats although no change in body wt. gain was noted. These results serve to clearly differentiate the metabolic finality of two distinct classes of drugs, as well as their corresponding nuclear receptors, having similar effects on serum triglycerides. (c) 2000 Academic Press.
 IT 213252-19-8, KRP 297
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological

study, unclassified); BIOL (Biological study)
 (fenofibrate and rosiglitazone lower serum triglycerides with opposing
 effects on body wt.)

RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 33 OF 42 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:243901 CAPLUS

DOCUMENT NUMBER: 133:12622

TITLE: Tissue-specific actions of antidiabetic thiazolidinediones on the reduced fatty acid oxidation in skeletal muscle and liver of zucker diabetic fatty rats

AUTHOR(S): Ide, Tomohiro; Nakazawa, Tomoko; Mochizuki, Toshiro; Murakami, Koji

CORPORATE SOURCE: Central Research Laboratories, Kyorin Pharmaceutical, Tochigi, 329-0114, Japan

SOURCE: Metabolism, Clinical and Experimental (2000), 49(4), 521-525

CODEN: METAAJ; ISSN: 0026-0495

PUBLISHER: W. B. Saunders Co.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Fatty acid overload has been proposed as a cause of decreased responsiveness in the major insulin target tissues of the body such as muscle and liver tissue. We therefore investigated fatty acid oxidn. in soleus muscle and liver isolated from Zucker diabetic fatty (ZDF) rats treated with thiazolidinediones, a new class of antidiabetic agents. ¹⁴CO₂ prodn. from [¹⁴C]palmitic (C16:0) acid was lower in the soleus muscle and liver of ZDF rats vs. lean rats (P < .05). When administered orally to ZDF rats for 2 wk, the thiazolidinediones troglitazone (300 mg/kg) and KRP-297 (10 mg/kg) increased palmitic acid oxidn. in the soleus muscle of ZDF rats (P < .05). KRP-297, but not troglitazone, increased palmitic acid oxidn. in the liver of ZDF rats (P < .05), and both troglitazone and KRP-297 inhibited triglyceride accumulation in the skeletal muscle of ZDF rats. Hepatic triglyceride accumulation in ZDF rats was inhibited by KRP-297, but not by troglitazone. A redn. of fatty acid oxidn. in the liver of ZDF rats and an increase in response to KRP-297 were obsd. only when C16:0 and C18:0 fatty acids, not C8:0, were

used as substrates. Thus, there were defects in fatty acid catabolic activity and triglyceride accumulation in the soleus muscle and liver of ZDF rats. These results indicate that KRP-297 has advantages over troglitazone in the amelioration of these lipid metabolic abnormalities in insulin resistance assocd. with obesity.

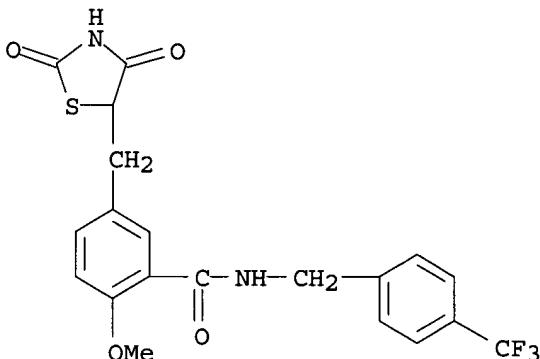
IT 213252-19-8, KRP-297

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(tissue-specific actions of antidiabetic thiazolidinediones on reduced fatty acid oxidn. in muscle and liver in NIDDM/obesity)

RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 34 OF 42 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:190928 CAPLUS

DOCUMENT NUMBER: 132:231969

TITLE: Method for treating diabetes employing an aP2 inhibitor and combination

INVENTOR(S): Robl, Jeffrey A.; Parker, Rex A.; Biller, Scott A.; Jamil, Haris; Jacobson, Bruce L.; Kodukula, Krishna

PATENT ASSIGNEE(S): Bristol-Myers Squibb Co., USA

SOURCE: PCT Int. Appl., 55 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2000015229 | A1 | 20000323 | WO 1999-US20946 | 19990913 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, | | | | |

ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG,
 CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
 CA 2344309 AA 20000323 CA 1999-2344309 19990913
 AU 9963877 A1 20000403 AU 1999-63877 19990913
 AU 754488 B2 20021114
 BR 9913833 A 20010529 BR 1999-13833 19990913
 EP 1121129 A1 20010808 EP 1999-951438 19990913
 R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
 IE, SI, LT, LV, FI, RO
 EE 200100154 A 20021216 EE 2001-20010015419990913
 NO 2001001351 A 20010511 NO 2001-1351 20010316
 LT 4871 B 20011227 LT 2001-22 20010316
 LT 4870 B 20011227 LT 2001-23 20010316
 LV 12686 B 20011020 LV 2001-57 20010412
 US 2002035064 A1 20020321 US 2001-905235 20010713
 PRIORITY APPLN. INFO.: US 1998-100677P P 19980917
 US 1999-390275 B1 19990907
 WO 1999-US20946 W 19990913

OTHER SOURCE(S): MARPAT 132:231969

AB A method is provided for treating diabetes and related diseases, such as insulin resistance, obesity, hyperglycemia, hyperinsulinemia, elevated blood levels of free fatty acids or glycerol, hypertriglyceridemia, and esp. Type II diabetes, employing an adipocyte protein aP2 inhibitor or a combination of an aP2 inhibitor and another antidiabetic agent such as metformin, glyburide, troglitazone and/or insulin.

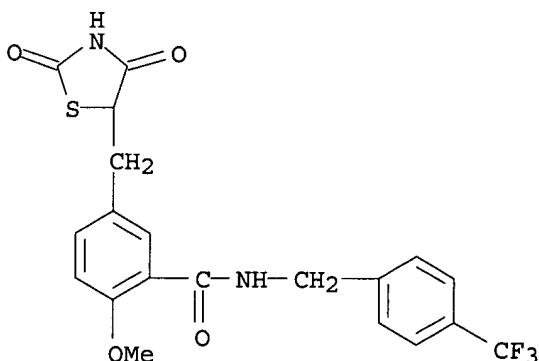
IT 213252-19-8, KRP 297

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(aP2 inhibitor and combination with another antidiabetic agent for treatment of diabetes and related diseases)

RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]-(9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 35 OF 42 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:751167 CAPLUS

DOCUMENT NUMBER: 132:44794

TITLE: Amelioration by KRP-297, a new thiazolidinedione, of impaired glucose uptake in skeletal muscle from obese

AUTHOR(S) : insulin-resistant animals
 Murakami, Koji; Tsunoda, Masaki; Ide, Tomohiro;
 Ohashi, Mitsuo; Mochizuki, Toshiro
 CORPORATE SOURCE: Central Research Laboratories, Kyorin Pharmaceutical
 Co Ltd., Tochigi, Japan
 SOURCE: Metabolism, Clinical and Experimental (1999), 48(11),
 1450-1454
 CODEN: METAAJ; ISSN: 0026-0495
 PUBLISHER: W. B. Saunders Co.
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB We examd. the effect of KRP-297, a new thiazolidinedione deriv., on glucose uptake in the soleus muscle of two animal models of insulin resistance that show moderate (ob/ob mice) and severe (db/db mice) hyperglycemia. Insulin-stimulated 2-deoxyglucose (2DG) uptake in soleus muscle was 53.8% lower in ob/ob mice vs. lean mice ($P < .05$). When administered to ob/ob mice, KRP-297 (0.3 to 10 mg/kg) decreased plasma glucose and insulin levels and improved the impaired insulin-stimulated 2DG uptake in soleus muscle in a dose-dependent manner. Soleus muscle from db/db mice exhibited defects in both basal (35.0% decrease, $P < .01$) and insulin-stimulated (50.5% decrease, $P < .01$) 2DG uptake. These defects were improved by treatment with KRP-297 (0.3 to 10 mg/kg). Moreover, KRP-297 prevented severe hyperglycemia and the marked decrease in pancreatic insulin content in db/db mice. These results suggest that KRP-297 treatment is useful to prevent the development of diabetic syndromes in addn. to ameliorating the impaired glucose transport in skeletal muscle.

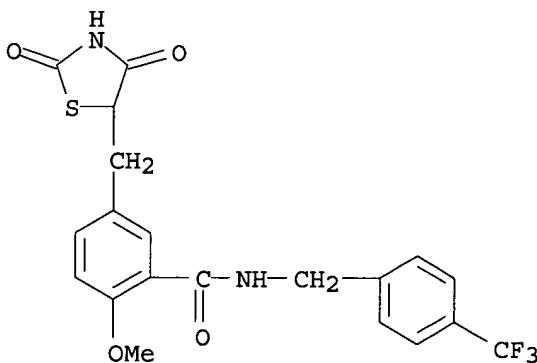
IT 213252-19-8, KRP-297

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(thiazolidinedione deriv. KRP-297 amelioration of impaired glucose uptake in skeletal muscle from obese insulin-resistant animals)

RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 36 OF 42 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 1999:436161 CAPLUS
 DOCUMENT NUMBER: 131:238315

TITLE: Evidence for direct binding of fatty acids and eicosanoids to human peroxisome proliferator-activated receptor .alpha.
 AUTHOR(S): Murakami, Koji; Ide, Tomohiro; Suzuki, Masahiro;
 Mochizuki, Toshiro; Kadokawa, Takashi
 CORPORATE SOURCE: Central Research Laboratories, Kyorin Pharmaceutical Co., Ltd., Tochigi, Japan
 SOURCE: Biochemical and Biophysical Research Communications (1999), 260(3), 609-613
 CODEN: BBRCA9; ISSN: 0006-291X
 PUBLISHER: Academic Press
 DOCUMENT TYPE: Journal
 LANGUAGE: English

AB The .alpha. isoform of peroxisome proliferator-activated receptor (PPAR) is activated by fatty acids, their metabolites, and the fibrate class of lipid-lowering agents. To test the ability of these activators to directly bind the ligand-binding domain of human PPAR.alpha., we performed a competitive binding assay using radiolabeled [3H]KRP-297, a known ligand for human PPAR.alpha.. Long-chain fatty acids and eicosanoids were even more potent ligands for human PPAR.alpha. than the hitherto most potent PPAR.alpha. ligand WY-14,643. Moreover, these natural ligands avidly activated this receptor in a transient transcriptional assay. This study provides the direct evidence that human PPAR.alpha. is activated through the direct binding of fatty acids and eicosanoids, as well as of a fibrate, to its ligand-binding domain. (c) 1999 Academic Press.

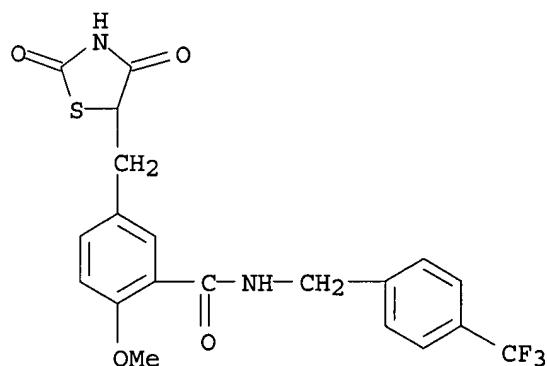
IT 213252-19-8, KRP-297

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)

(direct binding of fatty acids and eicosanoids to human peroxisome proliferator-activated receptor .alpha.)

RN 213252-19-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

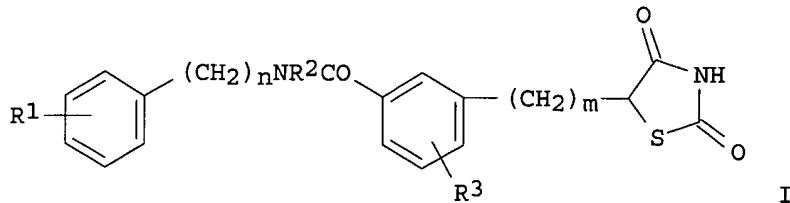
L4 ANSWER 37 OF 42 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1999:188591 CAPLUS

DOCUMENT NUMBER: 130:311725

TITLE: (3-Substituted benzyl)thiazolidine-2,4-diones as structurally new antihyperglycemic agents

AUTHOR(S) : Nomura, Masahiro; Kinoshita, Susumu; Sato, Hiroya;
 Maeda, Toshio; Murakami, Koji; Tsunoda, Masaki;
 Miyachi, Hiroyuki; Awano, Katsuya
 CORPORATE SOURCE: Central Research Laboratories, Kyorin Pharmaceutical
 Co., Ltd., Tochigi, 329-0114, Japan
 SOURCE: Bioorganic & Medicinal Chemistry Letters (1999), 9(4),
 533-538
 CODEN: BMCLE8; ISSN: 0960-894X
 PUBLISHER: Elsevier Science Ltd.
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB Title compds. I (R1 = 4-tert-Bu, H, 4-Me, 4-MeO, 4-CF₃, etc.; R2 = H, Et; R3 = 6-MeO, 4-MeO, 2-MeO, 6-EtO, 6-OH, 6-F, etc.; m = 0-3; n = 0-2) were prepd. A structure-activity study of these compds. led to the identification of I (R1 = CF₃, R2 = H, R3 = 6-MeO, m = n = 1) (KRP-297) as a candidate drug for the treatment of diabetes mellitus.

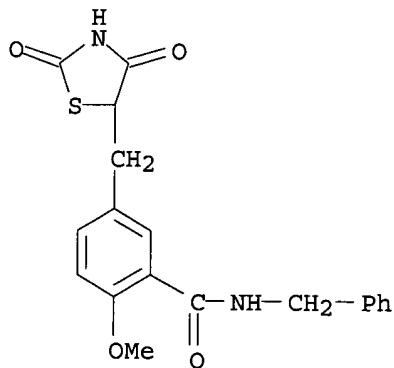
IT 185808-38-2P 185808-40-6P 185808-42-8P
 185808-45-1P 185808-49-5P 185808-51-9P
 185808-52-0P 185808-55-3P 185808-59-7P
 185808-62-2P 185808-63-3P 185808-64-4P
 185808-65-5P 185808-67-7P 185808-68-8P
 185808-70-2P 186312-86-7P 213252-19-8P,
 KRP-297 223508-81-4P 223508-82-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(prepn. and antihyperglycemic activity of)

RN 185808-38-2 CAPLUS

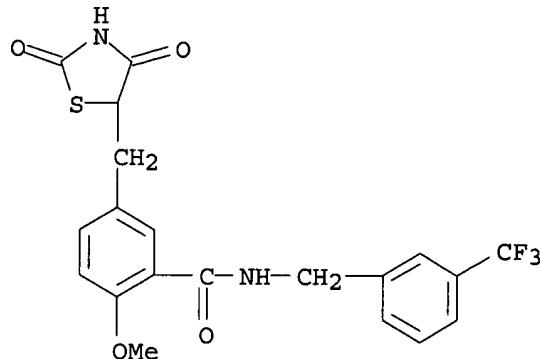
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



10049937

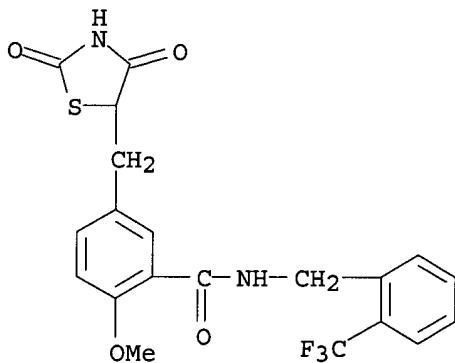
RN 185808-40-6 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(3-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



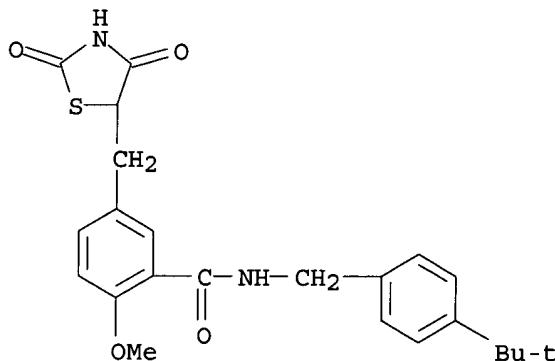
RN 185808-42-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(2-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



RN 185808-45-1 CAPLUS

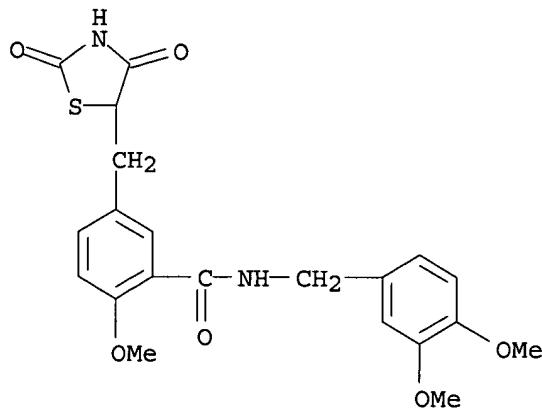
CN Benzamide, N-[(4-(1,1-dimethylethyl)phenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)



10049937

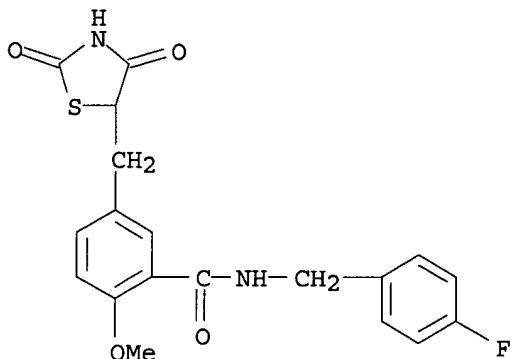
RN 185808-49-5 CAPLUS

CN Benzamide, N-[(3,4-dimethoxyphenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)



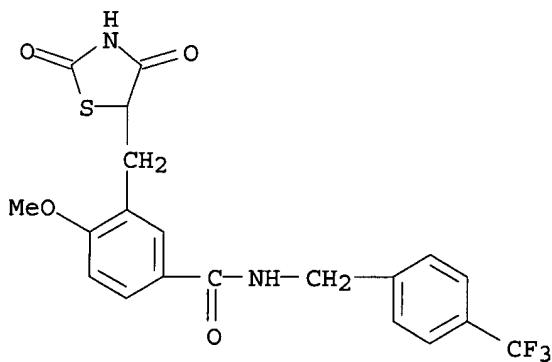
RN 185808-51-9 CAPLUS

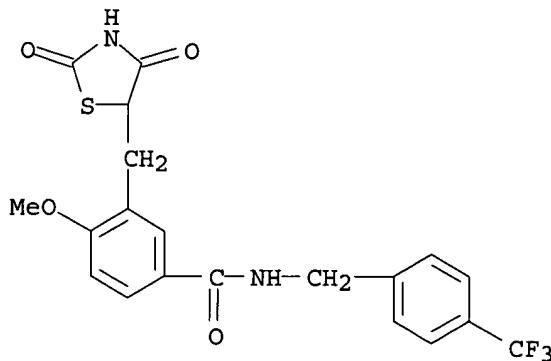
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-N-[(4-fluorophenyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)



RN 185808-52-0 CAPLUS

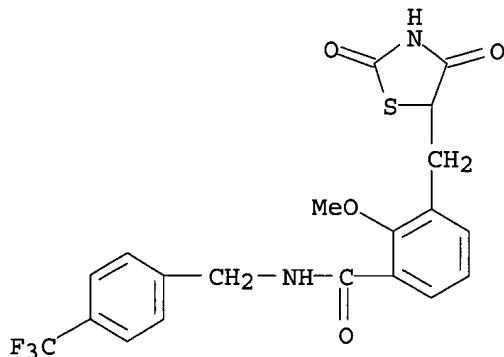
CN Benzamide, 3-[(2,4-dioxo-5-thiazolidinyl)methyl]-4-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)





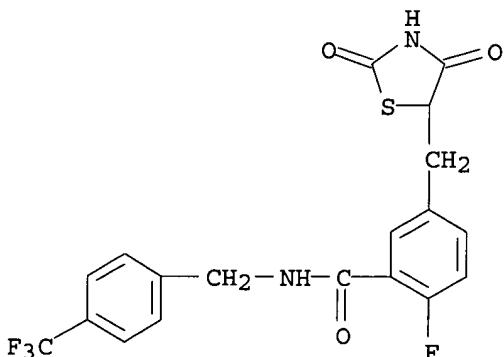
RN 185808-55-3 CAPLUS

CN Benzamide, 3-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



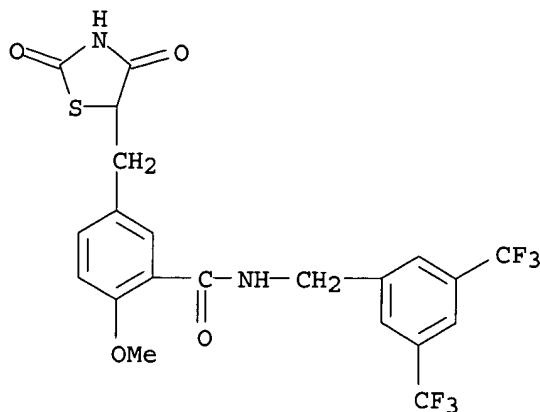
RN 185808-59-7 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-fluoro-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



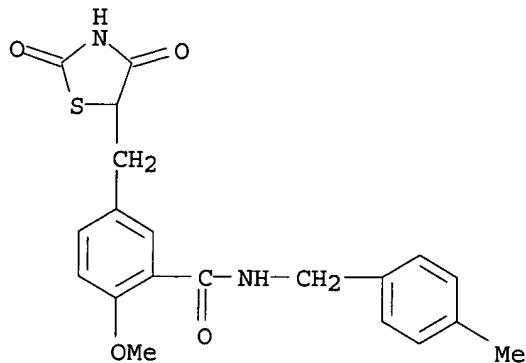
RN 185808-62-2 CAPLUS

CN Benzamide, N-[[3,5-bis(trifluoromethyl)phenyl]methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)



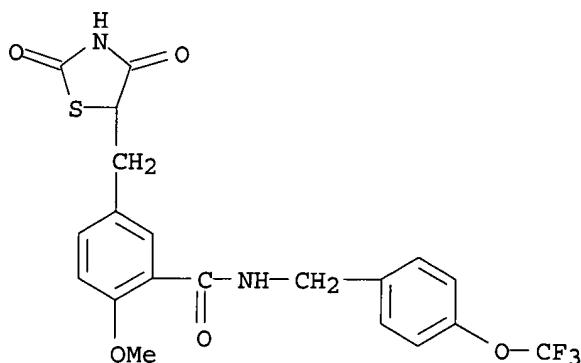
RN 185808-63-3 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-methylphenyl)methyl]- (9CI) (CA INDEX NAME)



RN 185808-64-4 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-trifluoromethoxyphenyl)methyl]- (9CI) (CA INDEX NAME)

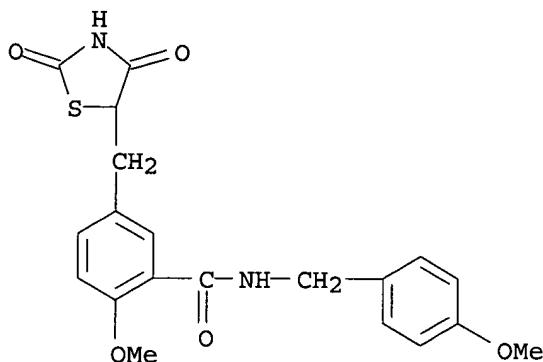


RN 185808-65-5 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-

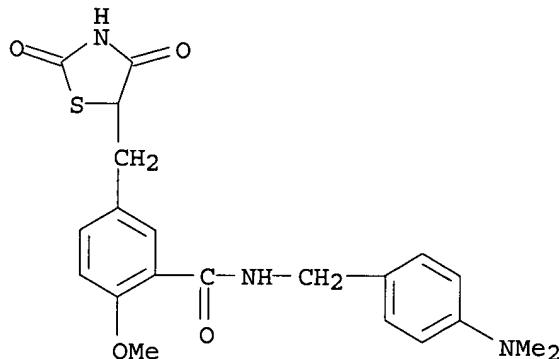
10049937

methoxyphenyl)methyl] - (9CI) (CA INDEX NAME)



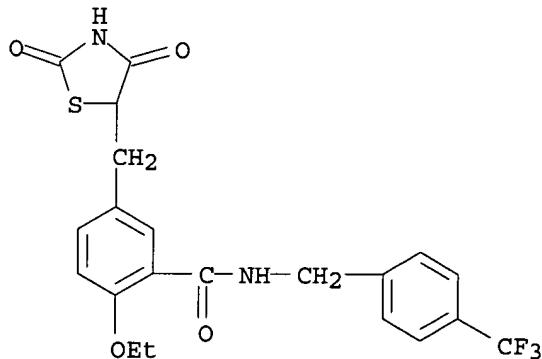
RN 185808-67-7 CAPLUS

CN Benzamide, N-[4-(dimethylamino)phenyl]methyl-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)



RN 185808-68-8 CAPLUS

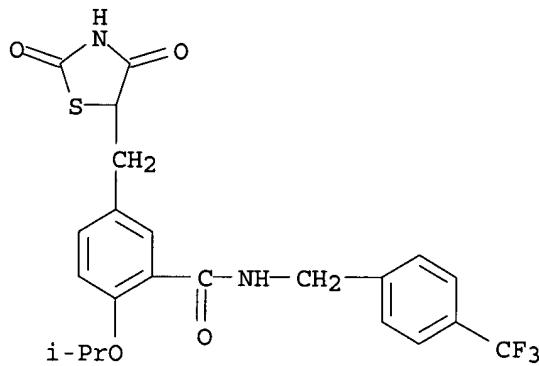
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-ethoxy-N-[4-(trifluoromethyl)phenyl]methyl] - (9CI) (CA INDEX NAME)



RN 185808-70-2 CAPLUS

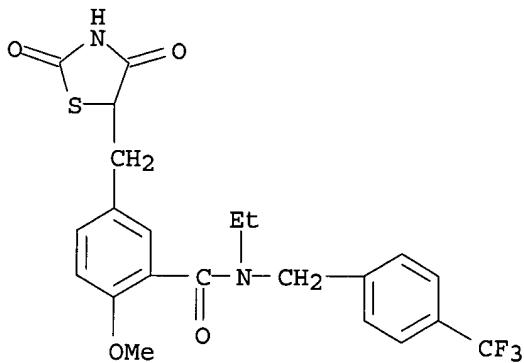
10049937

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-(1-methylethoxy)-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



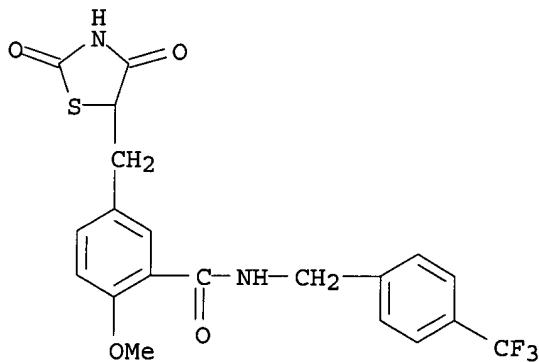
RN 186312-86-7 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-N-ethyl-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



RN 213252-19-8 CAPLUS

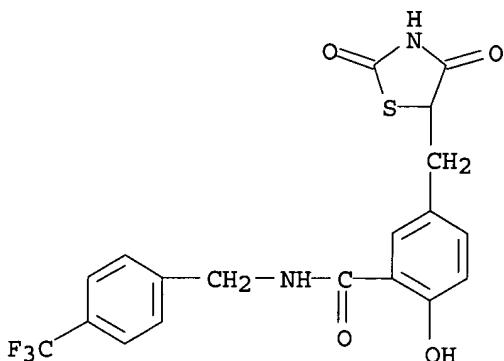
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



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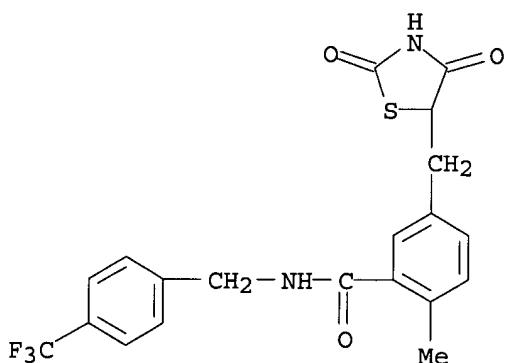
RN 223508-81-4 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-hydroxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



RN 223508-82-5 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methyl-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT:

15 THERE ARE 15 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 38 OF 42 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 1998:784882 CAPLUS

DOCUMENT NUMBER: 130:148506

TITLE: A novel insulin sensitizer acts as a coligand for peroxisome proliferator-activated receptor-.alpha. (PPAR-.alpha.) and PPAR-.gamma.: effect of PPAR-.alpha. activation on abnormal lipid metabolism in liver of Zucker fatty rats

AUTHOR(S): Murakami, Koji; Tobe, Kazuyuki; Ide, Tomohiro; Mochizuki, Toshiro; Ohashi, Mitsuo; Akanuma, Yasuo; Yazaki, Yoshio; Kadokawa, Takashi

CORPORATE SOURCE: Third Department of Internal Medicine, Faculty of Medicine, University of Tokyo, Tokyo, 113, Japan

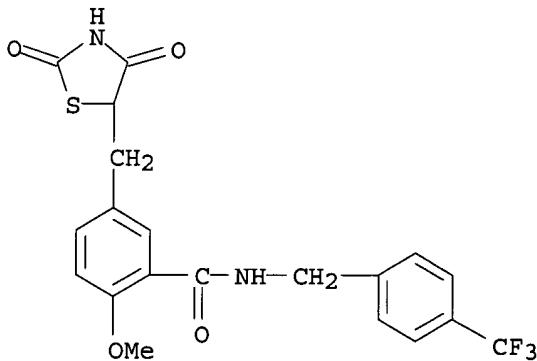
SOURCE: Diabetes (1998), 47(12), 1841-1847

CODEN: DIAEAZ; ISSN: 0012-1797

PUBLISHER: American Diabetes Association

DOCUMENT TYPE: Journal
 LANGUAGE: English
 AB We investigated the biol. activity of a novel thiazolidinedione (TZD) deriv., KRP-297, and the mol. basis of this activity. When administered to obese Zucker fatty rats (obese rats) at 10 mg/kg for 2 wk, KRP-297, unlike BRL-49653, restored reduced lipid oxidn., i.e., CO₂ and ketone body prodn. from [¹⁴C]palmitic acid, in the liver by 39% (P < 0.05) and 57% (P < 0.01), resp. KRP-297 was also significantly more effective than BRL-49653 in the inhibition of enhanced lipogenesis and triglyceride accumulation in the liver. To understand the mol. basis of the biol. effects of KRP-297, we examd. the effect on peroxisome proliferator-activated receptor (PPAR) isoforms, which may play key roles in lipid metab. Unlike classical TZD derivs., KRP-297 activated both PPAR-.alpha. and PPAR-.gamma., with median effective concns. of 1.0 and 0.8 .mu.mol/L, resp. Moreover, radiolabeled [³H]KRP-297 bound directly to PPAR-.alpha. and PPAR-.gamma. with dissocn. consts. of 228 and 326 nmol/L, resp. Concomitantly, KRP-297, but not BRL-49653, increased the mRNA and the activity (1.5-fold [P < 0.01] and 1.8-fold [P < 0.05], resp.) of acyl-CoA oxidase, which has been reported to be regulated by PPAR-.alpha., in the liver. By contrast, KRP-297 (P < 0.05) was less potent than BRL-49653 (P < 0.01) in inducing the PPAR-.gamma.-regulated aP2 gene mRNA expression in the adipose tissues. These results suggest that PPAR-.alpha. agonism has a protective effect against abnormal lipid metab. in liver of obese rats.

IT 213252-19-8, KRP 297
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (effect of PPAR-.alpha. activation by insulin sensitizer,
 thiazolidinedione deriv. KRP-297, on abnormal lipid metab. in liver of
 Zucker fatty rats)
 RN 213252-19-8 CAPLUS
 CN Benzamide, 5-[{(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-
 (trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 39 OF 42 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 1998:421607 CAPLUS
 DOCUMENT NUMBER: 129:239719
 TITLE: Effects of PPAR.alpha. activation on liver lipid metabolism in Zucker fatty rats

AUTHOR(S) : Ide, Tomohiro; Murakami, Koji; Tobe, Kazuyuki;
 Mochizuki, Toshiro; Ohashi, Mitsuo; Akanuma, Yasuo;
 Kadowaki, Takashi; Yazaki, Yoshio

CORPORATE SOURCE: Cent. Res. Lab., Kyorin Pharm. Co., Ltd., Tochigi,
 329-01, Japan

SOURCE: Diabetes Frontier (1998), 9(3), 345-346
 CODEN: DIFREZ; ISSN: 0915-6593

PUBLISHER: Medikaru Rebyusha

DOCUMENT TYPE: Journal

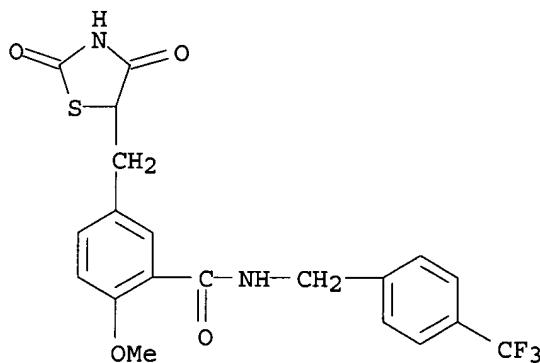
LANGUAGE: Japanese

AB Oral administration of KRP-297 or BRL-49653 with high affinity to PPAR .alpha. to Zucker fatty (obese) rats and to control lean rats for 2 wk significantly lowered the blood glucose, insulin, triglyceride, and free fatty acid levels in the obese rats. KRP-297 and BRL-49653 also suppressed the increase in triglyceride accumulation and fatty acid biosynthesis activity in the liver of the obese rats as compared to the lean rats. In contrast, the markedly reduced activity of the hepatic acyl-CoA oxidase in the obese rats was markedly recovered by the administration. The results suggest that the activation of PPAR .alpha. by KRP-297 or BRL-49653 (ligand) might have inhibitory action on the hepatic triglyceride accumulation and lipid metab. abnormality in the obese rats.

IT 213252-19-8, KRP 297
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
 (effects of PPAR.alpha. activation on liver lipid metab. in Zucker fatty rats)

RN 213252-19-8 CAPLUS

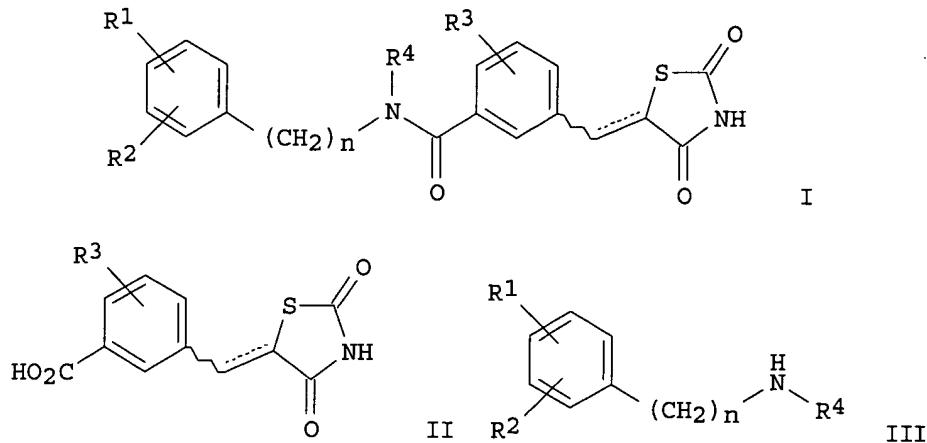
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 40 OF 42 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 1997:116453 CAPLUS
 DOCUMENT NUMBER: 126:157499
 TITLE: Preparation of N-substituted dioxothiazolidylbenzamide derivatives as blood sugar lowering agents
 INVENTOR(S) : Maeda, Toshio; Nomura, Masahiro; Awano, Katsuya;
 Kinoshita, Susumu; Sato, Hiroya; Murakami, Koji;
 Tsunoda, Masaki
 PATENT ASSIGNEE(S) : Kyorin Seiyaku Kk, Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 11 pp.
 CODEN: JKXXAF

DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|-------------------|-----------------|----------|
| JP 08333355 | A2 | 19961217 | JP 1995-159782 | 19950602 |
| PRIORITY APPLN. INFO.: | | | JP 1995-159782 | 19950602 |
| OTHER SOURCE(S): | | MARPAT 126:157499 | | |
| GI | | | | |



AB The title compds. (I; R1, R2 = H, C1-4 alkyl, C1-3 alkoxy, haloalkoxy, or haloalkyl, halo, OH, NO₂, etc.; R3 = H, C1-3 alkoxy, halo, OH; R4 = H, C1-4 alkyl; dotted line = single or double bond; n = 0-2) are prep'd. by reacting benzoic acid derivs. (II; R3, dotted line = same as above) with amines (III; R1, R2, R4, n = same as above). I, possessing blood sugar and lipid lowering activities, are useful for diabetes mellitus and hyperlipemia. Thus, 5-(2,4-dioxothiazolidyl-5-ylidene)methyl-2-methoxybenzoic acid was reacted with 4-tert-butylaniline in the presence of Et₃N and NCP(O)(OEt)₂ to give 99% I (R1 = 4-tert-BuC₆H₄, R3 = 2-MeO, R2 = R4 = H, dotted line = double bond, n = 0). I (R1 = R2 = 4-CF₃, R3 = 6-MeO, R4 = Et, dotted line = single bond, n = 1) at 10 mg/kg showed 31% blood sugar lowering activity when tested on mouses p.o. in vivo.

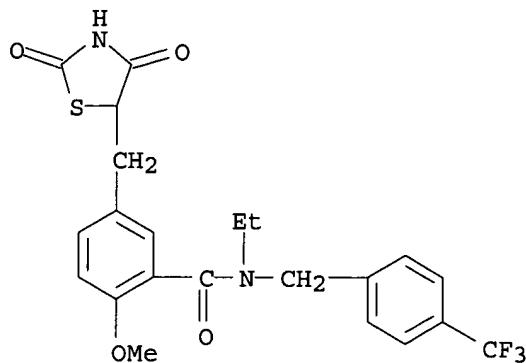
IT 186312-86-7P 186312-87-8P 186312-89-0P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of N-substituted dioxothiazolidylbenzamide derivs. as blood sugar lowering agents)

RN 186312-86-7 CAPLUS

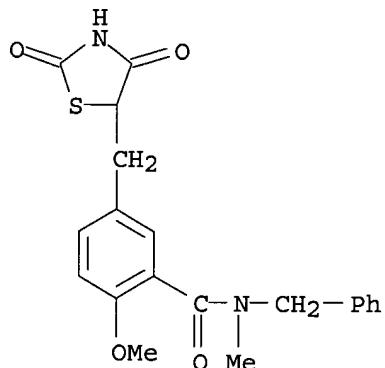
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-N-ethyl-2-methoxy-N-[4-(trifluoromethyl)phenyl]methyl]- (9CI) (CA INDEX NAME)

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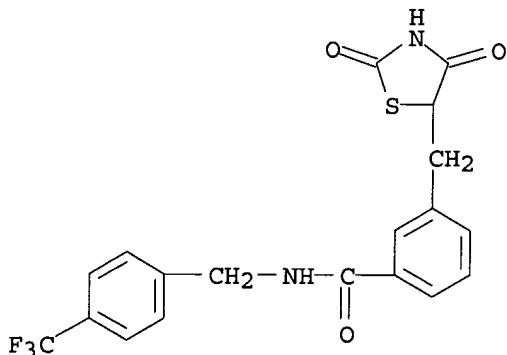
RN 186312-87-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-methyl-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 186312-89-0 CAPLUS

CN Benzamide, 3-[(2,4-dioxo-5-thiazolidinyl)methyl]-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



L4 ANSWER 41 OF 42 CAPLUS COPYRIGHT 2003 ACS

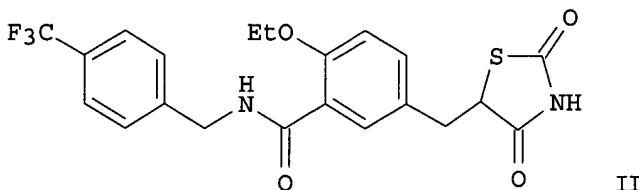
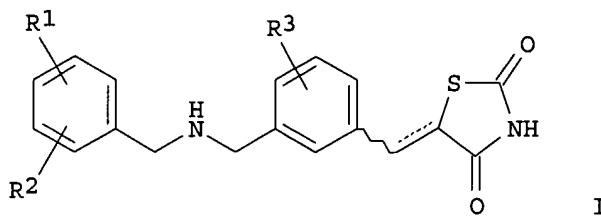
ACCESSION NUMBER: 1997:85180 CAPLUS

DOCUMENT NUMBER: 126:104076

TITLE: Preparation of N-benzyldioxothiazolidylbenzamide derivatives as antidiabetics and hypolipemics
 INVENTOR(S): Maeda, Toshio; Nomura, Masahiro; Awano, Katsuya; Kinoshita, Susumu; Satoh, Hiroya; Murakami, Koji; Tsunoda, Masaki
 PATENT ASSIGNEE(S): Kyorin Pharmaceutical Co., Ltd., Japan; Maeda, Toshio; Nomura, Masahiro; Awano, Katsuya; Kinoshita, Susumu; Satoh, Hiroya; Murakami, Koji; Tsunoda, Masaki
 SOURCE: PCT Int. Appl., 40 pp.
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|------------------|------------|
| WO 9638428 | A1 | 19961205 | WO 1996-JP1459 | 19960530 |
| W: AU, CA, CN, HU, KR, US | | | | |
| RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE | | | | |
| JP 09048771 | A2 | 19970218 | JP 1996-153139 | 19960524 |
| JP 3144624 | B2 | 20010312 | | |
| JP 2001139565 | A2 | 20010522 | JP 2000-350367 | 19960524 |
| CA 2220698 | AA | 19961205 | CA 1996-2220698 | 19960530 |
| AU 9658446 | A1 | 19961218 | AU 1996-58446 | 19960530 |
| AU 698896 | B2 | 19981112 | | |
| EP 846693 | A1 | 19980610 | EP 1996-920002 | 19960530 |
| EP 846693 | B1 | 20020123 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| CN 1186489 | A | 19980701 | CN 1996-194390 | 19960530 |
| CN 1069901 | B | 20010822 | | |
| AT 212341 | E | 20020215 | AT 1996-920002 | 19960530 |
| ES 2170858 | T3 | 20020816 | ES 1996-920002 | 19960530 |
| TW 400328 | B | 20000801 | TW 1996-85106555 | 19960601 |
| US 6030990 | A | 20000229 | US 1997-952672 | 19971202 |
| US 6001862 | A | 19991214 | US 1999-292955 | 19990416 |
| US 6147101 | A | 20001114 | US 2000-482268 | 20000113 |
| CN 1336366 | A | 20020220 | CN 2000-130138 | 20001017 |
| PRIORITY APPLN. INFO.: | | | JP 1995-159781 | A 19950602 |
| | | | JP 1996-153139 | A 19960524 |
| | | | WO 1996-JP1459 | W 19960530 |

OTHER SOURCE(S) : MARPAT 126:104076
 GI



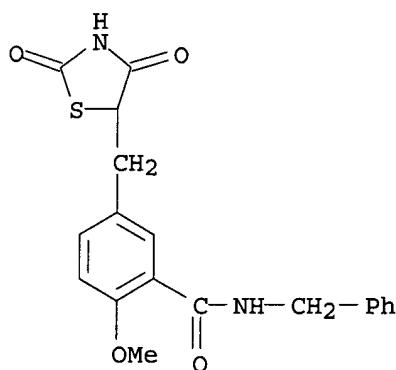
AB Novel N-benzylidioxothiazolidylbenzamide derivs. represented by general formula I [R1 and R2 are the same or different and each represents hydrogen, lower (C1-4) alkyl, lower (C1-3) alkoxy, lower (C1-3) haloalkyl, lower (C1-3) haloalkoxy, halogeno, hydroxy, nitro, amino optionally substituted by lower (C1-3) alkyl or a heterocycle, or R1 and R2 may be bonded to each other to form methylenedioxy; R3 represents lower (C1-3) alkoxy, hydroxy or halogeno; and the dotted line represents a double or single bond] are prepd. The title compd. II at 10 mg/kg gave 37% decrease in blood sugar in obese mice.

IT 185808-38-2P 185808-40-6P 185808-42-8P
 185808-45-1P 185808-49-5P 185808-51-9P
 185808-52-0P 185808-54-2P 185808-55-3P
 185808-59-7P 185808-62-2P 185808-63-3P
 185808-64-4P 185808-65-5P 185808-67-7P
 185808-68-8P 185808-70-2P 185808-71-3P
185808-72-4P 185808-73-5P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (prepn. of N-benzylidioxothiazolidylbenzamide derivs. as antidiabetics and hypolipemics)

RN 185808-38-2 CAPLUS

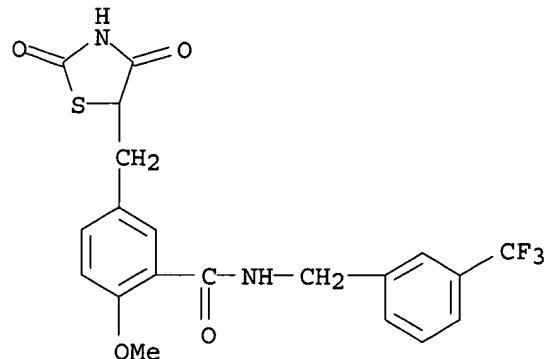
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



10049937

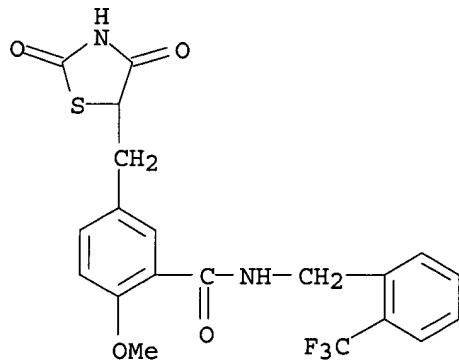
RN 185808-40-6 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(3-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



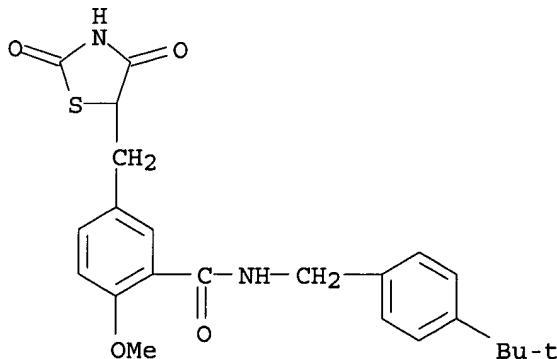
RN 185808-42-8 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(2-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



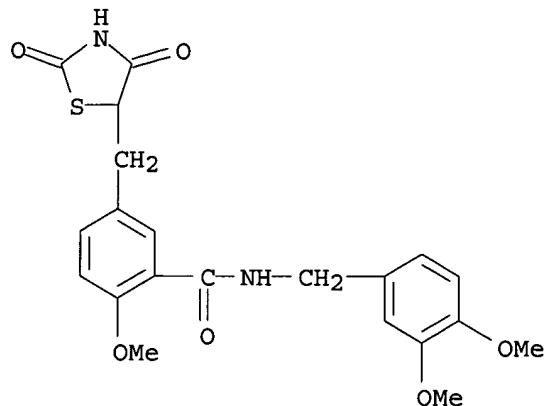
RN 185808-45-1 CAPLUS

CN Benzamide, N-[(4-(1,1-dimethylethyl)phenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)

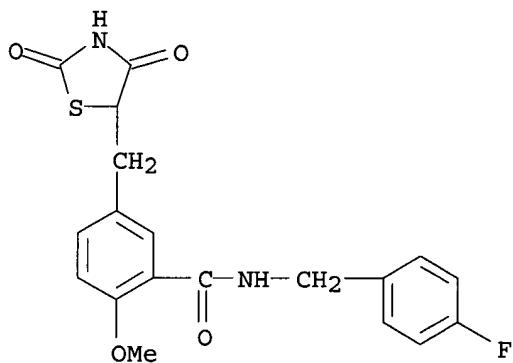


10049937

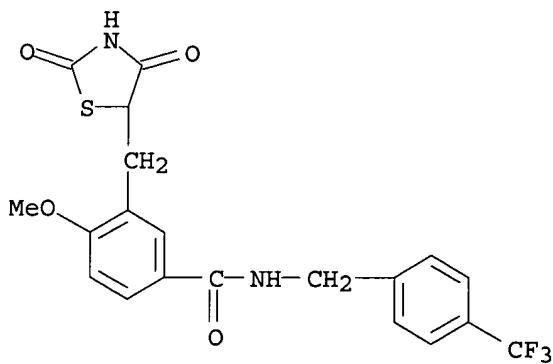
RN 185808-49-5 CAPLUS
CN Benzamide, N-[(3,4-dimethoxyphenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)

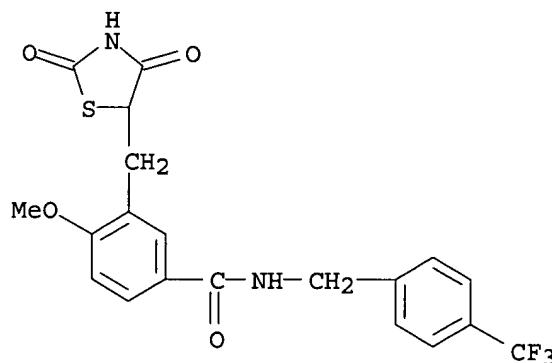


RN 185808-51-9 CAPLUS
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-N-[(4-fluorophenyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)

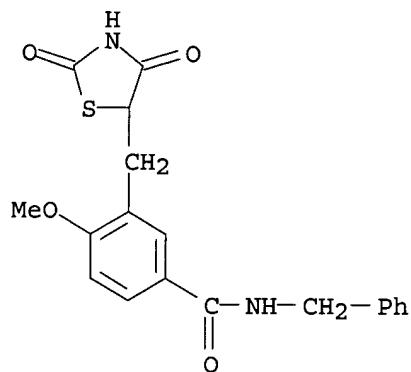


RN 185808-52-0 CAPLUS
CN Benzamide, 3-[(2,4-dioxo-5-thiazolidinyl)methyl]-4-methoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)

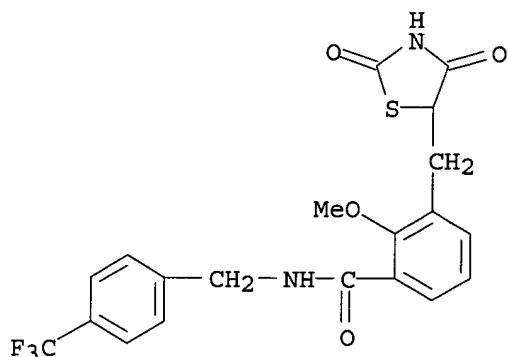




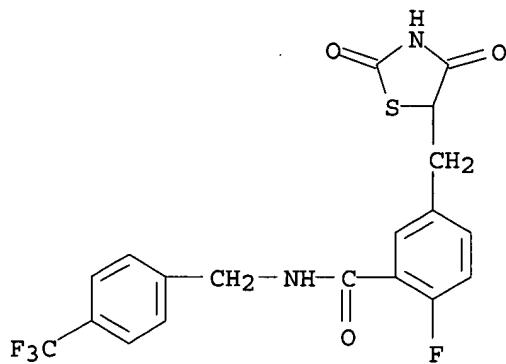
RN 185808-54-2 CAPLUS
 CN Benzamide, 3-[(2,4-dioxo-5-thiazolidinyl)methyl]-4-methoxy-N-(phenylmethyl)- (9CI) (CA INDEX NAME)



RN 185808-55-3 CAPLUS
 CN Benzamide, 3-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-trifluoromethylphenyl)methyl]- (9CI) (CA INDEX NAME)

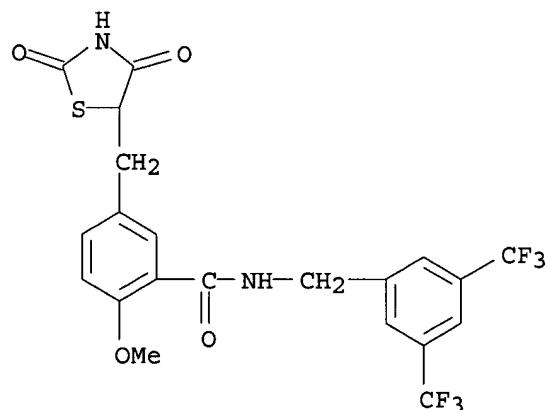


RN 185808-59-7 CAPLUS
 CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-fluoro-N-[(4-trifluoromethylphenyl)methyl]- (9CI) (CA INDEX NAME)



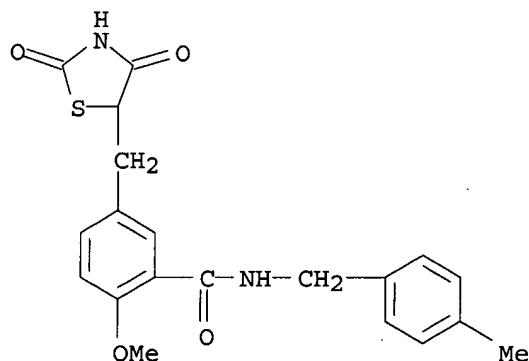
RN 185808-62-2 CAPLUS

CN Benzamide, N-[3,5-bis(trifluoromethyl)phenyl]methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)



RN 185808-63-3 CAPLUS

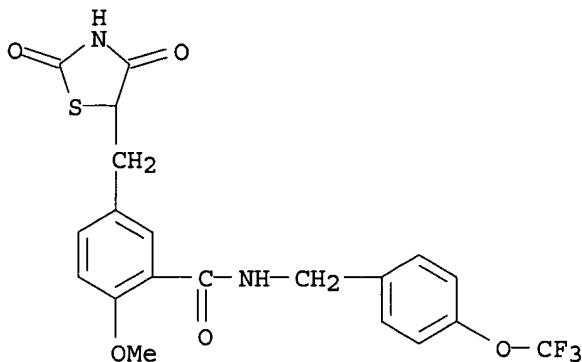
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-methylphenyl)methyl]- (9CI) (CA INDEX NAME)



RN 185808-64-4 CAPLUS

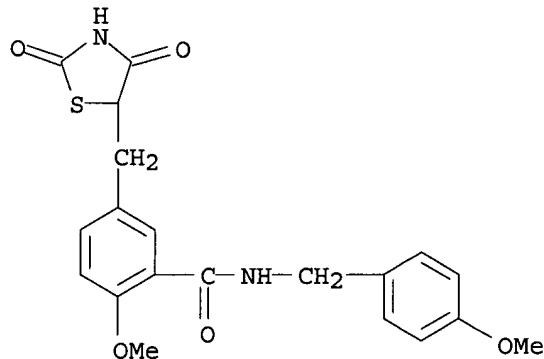
CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-

(trifluoromethoxy)phenyl]methyl]- (9CI) (CA INDEX NAME)



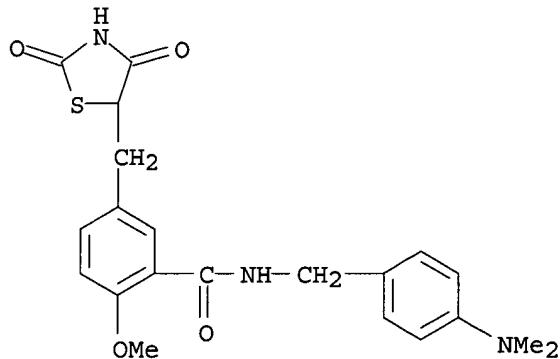
RN 185808-65-5 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[(4-methoxyphenyl)methyl]- (9CI) (CA INDEX NAME)



RN 185808-67-7 CAPLUS

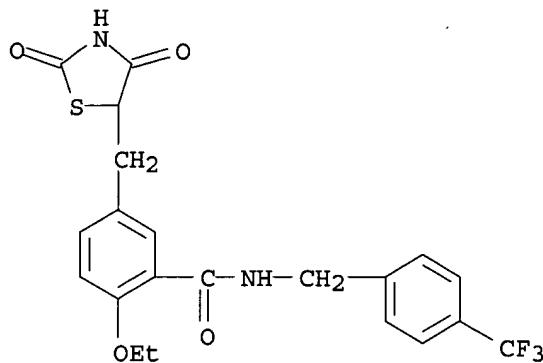
CN Benzamide, N-[(4-(dimethylamino)phenyl)methyl]-5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy- (9CI) (CA INDEX NAME)



RN 185808-68-8 CAPLUS

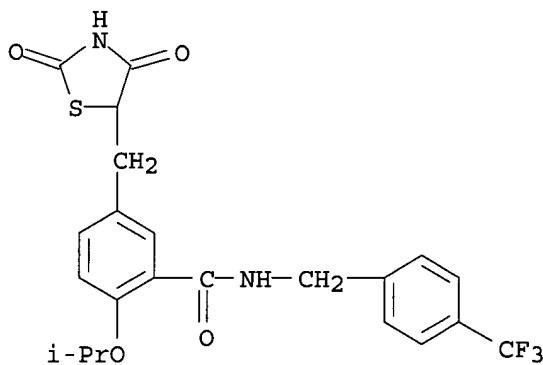
10049937

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-ethoxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



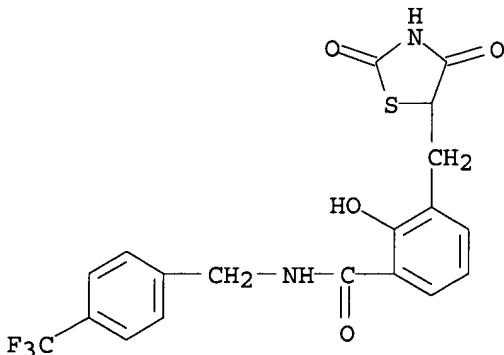
RN 185808-70-2 CAPLUS

CN Benzamide, 5-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-(1-methylethoxy)-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



RN 185808-71-3 CAPLUS

CN Benzamide, 3-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-hydroxy-N-[(4-(trifluoromethyl)phenyl)methyl]- (9CI) (CA INDEX NAME)



10049937

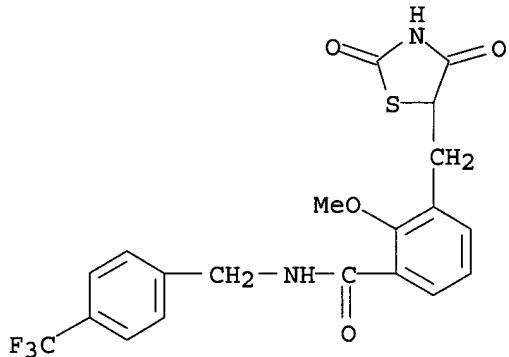
RN 185808-72-4 CAPLUS

CN Benzamide, 3-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]-, compd. with (S)-.alpha.-methylbenzenemethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 185808-55-3

CMF C20 H17 F3 N2 O4 S

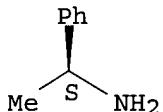


CM 2

CRN 2627-86-3

CMF C8 H11 N

Absolute stereochemistry.



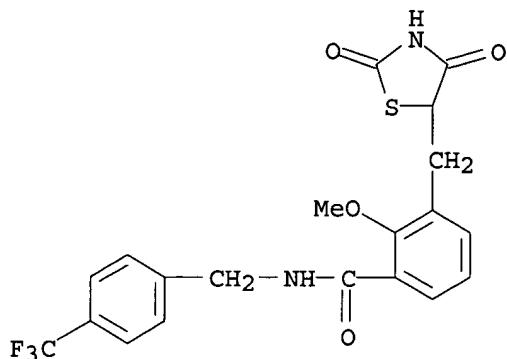
RN 185808-73-5 CAPLUS

CN Benzamide, 3-[(2,4-dioxo-5-thiazolidinyl)methyl]-2-methoxy-N-[[4-(trifluoromethyl)phenyl]methyl]-, compd. with (R)-.alpha.-methylbenzenemethanamine (1:1) (9CI) (CA INDEX NAME)

CM 1

CRN 185808-55-3

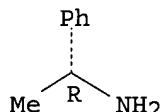
CMF C20 H17 F3 N2 O4 S



CM 2

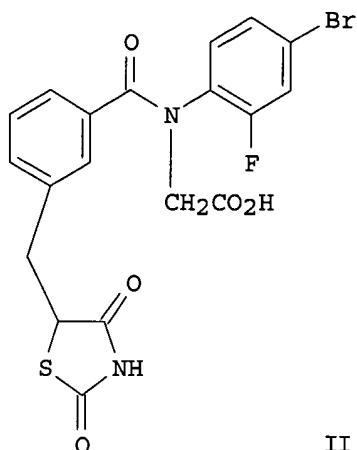
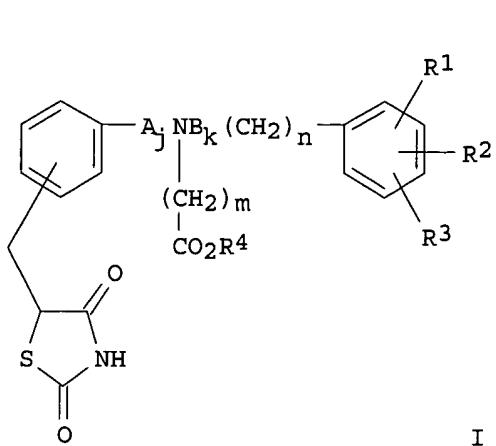
CRN 3886-69-9
CMF C8 H11 N

Absolute stereochemistry.



L4 ANSWER 42 OF 42 CAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 1996:537365 CAPLUS
 DOCUMENT NUMBER: 125:195637
 TITLE: Preparation of dioxothiazolidine derivatives as hypoglycemics and aldose reductase inhibitors
 INVENTOR(S): Matsushima, Hiroaki; Sugizaki, Myoshi; Myaoka, Shozo
 PATENT ASSIGNEE(S): Terumo Corp, Japan
 SOURCE: Jpn. Kokai Tokkyo Koho, 31 pp.
 CODEN: JKXXAF
 DOCUMENT TYPE: Patent
 LANGUAGE: Japanese
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|-------------------|-----------------|----------|
| JP 08143556 | A2 | 19960604 | JP 1994-280957 | 19941115 |
| PRIORITY APPLN. INFO.: | | | JP 1994-280957 | 19941115 |
| OTHER SOURCE(S): | | MARPAT 125:195637 | | |
| GI | | | | |



AB The title compds. I [A, B = carbonyl, etc.; R4 = H, alkyl; R1 - R3 = H, halo, etc.; j, k = 0 or 1; m = 1 or 2; n = 0 or 1] are prep'd. The title compd. II (prepn. given) in vitro showed IC50 of 8.32×10^{-7} M against aldose reductase. II also showed hypoglycemic activity.

IT 180631-42-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(prepn. of dioxothiazolidine derivs. as hypoglycemics and aldose reductase inhibitors)

RN 180631-42-9 CAPLUS

CN Glycine, N-[(4-bromo-2-fluorophenyl)methyl]-N-[3-[(2,4-dioxo-5-thiazolidinyl)methyl]benzoyl]- (9CI) (CA INDEX NAME)

